From: Carr, Sarah (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/CN=OD/CN=CARRS]
Sent: 12/23/2016 5:35:58 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]
Subject: RE: NIST's proposed response to KEI comments on regs

yes

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Friday, December 23, 2016 10:54 AM
To: Carr, Sarah (NIH/OD) [E] <CarrS@OD.NIH.GOV>
Subject: NIST's proposed response to KEI comments on regs

I think this is ok, you?

b5

Mark L. Rohrbaugh, Ph.D., J.D.
Special Advisor for Technology Transfer
Director, Division of Technology Transfer and Innovation Policy
Office of Science Policy
Office of the Director
National Institutes of Health

From: Rodriguez, Richard (NIH/NCI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=8092CB5394E04733AC0D4D84D25F65E5-RODRIGR]
Sent: 2/26/2018 3:06:17 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: KEI

Hi Mark,

I know you've been on travel but I'd like to set up a time for you and I to talk to Dale about responding to KEI. Please let me know when you would have some time.

Thanks,

Richard

RICHARD U. RODRIGUEZ, M.B.A.
Associate Director
Patent Agent

Technology Transfer Center
National Cancer Institute
National Institutes of Health
9609 Medical Center Drive, Rm 1E530
Bethesda, MD 20892-9702 (for business mail)
Rockville, MD 20850-9702 (for courier service/visitors)
Phone (Main Office): 240-276-5530
Direct phone: 240-276-6661
Fax 240-276-5504
richard.rodriguez@nih.gov

https://techtransfer.cancer.gov

"Start by doing what's necessary; then do what's possible; and suddenly you are doing the impossible" - Francis of Assisi

Note: This email may contain confidential information. If you are not the intended recipient, any disclosure, copying or use of this email or the information enclosed therein is strictly prohibited, and you should notify the sender for return of any attached documents.

From: Gottesman, Michael (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=918C2344931542A592D00DBE83D3D5A3-GOTTESMM]
Sent: 2/23/2018 11:29:05 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: Re: Licensing problem

Thanks, Mark. b5
Michael

From: "Rohrbaugh, Mark (NIH/OD) [E]" <rohrbaum@od.nih.gov>
Date: Friday, February 23, 2018 at 1:42 PM
To: "Gottesman, Michael (NIH/OD) [E]" <gottesmm@mail.nih.gov>
Subject: Re: Licensing problem

It is KEI, which opposes every single exclusive license notice that goes out. b5 b5 I will check in with NCI.

Sent from my iPhone

On Feb 23, 2018, at 1:36 PM, Gottesman, Michael (NIH/OD) [E] <gottesmm@mail.nih.gov> wrote:

> Ira,
> I hadn't heard this, but will check.
> Michael
>
> ---
>
> **From:** "Pastan, Ira (NIH/NCI) [E]" <pastani@mail.nih.gov>
> **Date:** Friday, February 23, 2018 at 10:43 AM
> **To:** "Gottesman, Michael (NIH/OD) [E]" <gottesmm@mail.nih.gov>
> **Subject:** Licensing problem
>
> Michael,
>
> b5
>
> Ira

From: Shmilovich, Michael (NIH/NHLBI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7DFE19BFD1D443CEB700B9F22D159A90-SHMILOVM]
Sent: 8/22/2019 6:16:30 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Berkley, Dale (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5ee461c29f5045a49f0adf82caaa2f31-berkleyd]; Pazman, Cecilia (NIH/NHLBI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=bf35741501e247d887acd224eaf9d679-pazmance]; Goldstein, Bruce (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cb67e8fe5aa2452a8a7f200e5fb4335b-goldsteb]
Subject: KEI MTTI ltr.docx
Attachments: KEI MTTI ltr.docx

Mark and Dale –
Here's my 2c.

Cecilia and Bruce- let me know what you think or if you have additional comments.

Regards,

Michael A. Shmilovich, Esq., CLP
NIH National Heart, Lung, and Blood Institute
Office of Technology Transfer and Development
31 Center Drive Room 4A29, MSC2479
Bethesda, MD 20892-2479
o. 301.435.5019
shmilovm@nih.gov

This message may contain privileged and confidential information intended only for the use of the individual(s) or entity named above. If you are not the intended recipient, you are hereby notified that any use, dissemination, distribution, or copying of this message or its content is strictly prohibited. If you have received this message in error, please notify sender immediately and destroy the message without making a copy. Thank you.

Dear Ms. Ardizzone:

b5

From: Joe Allen [jallen@allen-assoc.com]
Sent: 12/24/2016 3:12:54 AM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]
Subject: First draft
Attachments: The National Cancer Institute Didn't Deserve Its Treatment in the NY Times.docx

I need to hone this down some more,so don't worry about general editing but I would appreciate your looking it over to see if the facts used in the rebuttal are correct.

Thanks

--

Joseph P. Allen
President
Allen and Associates
60704 Rt. 26, South
Bethesda, OH 43719
(W) 740-484-1814
(c) b6
www.allen-assoc.com

The National Cancer Institute Didn't Deserve Its Treatment in the New York Times

By Joseph P. Allen

Imagine that you had found a drug at a government lab that promises to cure, not just treat certain blood cancers. Even better, suppose you started a new company taking on the big boys while building a state of the art manufacturing facility to make the drug in the US. As cherry on top, how about if the drug was being developed under a partnership as encouraged by every President from Ronald Reagan to Barack Obama? Sounds like you did something deserving public praise. Now imagine you're a researcher at the National Cancer Institute (NCI, part of the National Institutes of Health) who's been working for years on what could be a breakthrough invention, knowing that it will never benefit those you are charged to protect unless you can find a commercial partner. Then after many years, you find a small company that shares your vision, co-founded by someone who spent time at NCI and deeply respects your research team. They go out and raise millions of dollars required to move the discovery from the lab into the marketplace. Additionally, you've negotiated an agreement which has brought additional funding into NCI to conduct research you would not otherwise be able to do. Further, if the invention is successful, the Institute will receive millions of additional research dollars and the lab inventors will receive a share of the royalties as required by law. Sounds like a grand slam for all parties, doesn't it? Now imagine how you'd feel after reading the New York Times article "Harnessing the U.S. Taxpayer to Fight Cancer and Make Profits" (http://www.nytimes.com/2016/12/19/health/harnessing-the-us-taxpayer-to-fight-cancer-and-make-profits.html?action=click&contentCollection=health&region=rank&module=package&version=highlights&contentPlacement=2&pgtype=sectionfront) that implies everyone involved committed a nefarious deed, betraying the public interest.

The NY Times has been on quite a roll lately (no, not talking about the letter from the Publisher/Executive Editor (http://www.nytimes.com/2016/11/13/us/elections/to-our-readers-from-the-publisher-and-executive-editor.html?_r=0) apologizing for its unfair election coverage). A week before this story, they ran a video "Lives and Profits in the Balance: The High Stakes of Medical Patents" (http://www.nytimes.com/2016/12/11/us/retro-report-medical-patents-profits.html) repeating the myth that the government is failing to use the authorities of the Bayh-Dole Act to control drug prices. That's a theme of the NCI story.

The issuance of these articles seems like part of the campaign applying pressure on NIH to misuse the Bayh-Dole Act for compulsory licenses against drugs deemed too expensive. Regardless of the intent, let's unbundle the implied charges about the partnership between Kite

Pharma and NCI to commercialize a promising immunotherapy discovery. Here are key quotes from the NY Times' story:

> *Kite's treatment, a form of immunotherapy called CAR-T, was initially developed by a team of researchers at the National Cancer Institute...*

Not only wasn't the drug "developed" by NCI-- it's not developed. The NCI research group first reported their discovery in 2009, followed a year later with mouse studies and a promising single patient study. NCI also reported data from an expanded clinical study involving eight patients. That's a long way from being a useful drug. Only because of Kite's financial backing, the drug is in Phase I testing. The odds of any drug going from there to the marketplace are well below 50%. This is the stage where the costs-- and risks-- of drug development increase exponentially. This burden falls squarely on Kite. The other drugs being developed in the partnership are not even at Phase I yet.

> *Kite's first drug, called KTE-C19, could help thousands of patients each year in the United States with certain blood cancers. If it succeeds, it could generate sales of $1 billion to $2 billion annually, according to Wall Street analysts, making it among the most lucrative drugs to come from government research.*

It "could generate sales of $1 billion to $2 billion annually"-- or it could generate nothing. It's too early to know if it's "among the most lucrative drugs to come from government research" or just another promising drug that died in clinical trials. When drugs that a company is built around fail, people lose their jobs and the company may go under. While we don't know the result yet, we do know that without companies like Kite these discoveries would wither away in the lab.

> *Defenders say that the partnership will likely bring a lifesaving treatment to patients, something the government cannot really do by itself, and that that is what matters most.*
>
> *Critics say that taxpayers will end up paying twice for the same drug — once to support its development and a second time to buy it — while the company reaps the financial benefit.*
>
> *"If this was not a government-funded cancer treatment — if it was for a new solar technology, for example — it would be scandalous to think that some private investors are reaping massive profits off a taxpayer-funded invention," said James Love, director of Knowledge Ecology International, an advocacy group concerned with access to medicines.*

This builds on the myth that the government is developing drugs. Federally funded inventions are early stage discoveries, far removed from being useful products. The risks and expense of commercial development fall on the private sector. In the case of drug development, these expenses often costs hundreds of millions or even billions of dollars with a very high failure rate. It was largely the concern that potentially important medical discoveries were wasting away that led Congress to enact the Bayh-Dole Act and the Federal Technology Transfer Act creating incentives for industry to partner with universities and federal labs so these discoveries could benefit taxpayers. They are not "paying twice for the same drugs" but finally have an avenue transforming publicly funded research into new products, jobs and companies benefitting the nation and the world.

> *The debate goes squarely to one of the nation's most vexing challenges: rising health care and drug prices. Kite is one of a growing number of drug and biotech companies relying on federal laboratories. Analysts expect the company to charge at least $200,000 for the new treatment, which is intended as a one-time therapy for patients.*
>
> *While the law allows the government to demand drug-price concessions from its private-sector partners, the government has declined to do so with Kite and generally disdains the practice.*

No, the law does not allow the government to control the price of drugs developed from university or federal lab licenses (see NIH Director Collins Stands Up to the March in Mob (http://www.ipwatchdog.com/2016/06/27/nih-director-collins-march-in-mob/id=70391/ and When Government Tried March In Rights to Control Health Care Costs (http://www.ipwatchdog.com/2016/05/02/march-in-rights-health-care-costs/id=68816/). The Bayh-Dole Act only allows agencies to "march-in" requiring compulsory licenses if good faith efforts are not being made to commercialize a federally funded invention or if the licensee cannot produce enough product to meet a national security or health emergency. Regardless, persistent efforts are underway to pressure NIH to misapply the law. That appears to be a goal of the NY Times.

> *Insisting on lower prices, federal researchers say, would drive away innovative partners that speed the drug-development process and benefit patients. But with the government doing so much pivotal research, others say that the private sector cannot afford to walk away.*
>
> *"The market is so reliant on the knowledge and know-how that comes out of the government and academic labs," said Dr. Aaron Kesselheim, director of the Program on Regulation, Therapeutics and Law at Brigham & Women's Hospital in Boston.*
>
> *Price curbs, he said, "would not suddenly lead to a total abandonment of this pipeline. It couldn't possibly."*

> *Drug makers would be especially unlikely to turn away from immunotherapy, where the promising science has set off a "gold rush mentality," according to Mark Edwards of Bioscience Advisors, a company which tracks pharmaceutical licensing deals.*

We've been down this road before. In 1989 NIH was pressured into including "reasonable pricing" language in its Cooperative R&D Agreements (CRADAS). The result-- companies walked away and the policy had to be rescinded (https://www.ott.nih.gov/policies-reports). Thinking that because industry sees universities and federal labs as reliable research partners means that we can pull the rug out from under them is not only immoral but short sided. China is targeting the life sciences, pouring billions into their research universities to challenge our lead in basic science. They would welcome with open arms US biotech and drug companies willing to relocate their research activities there. Of course, they are also capable of pulling their own bait and switch after pumping our companies of their expertise.

> *Kite's first drug, called KTE-C19, could help thousands of patients each year in the United States with certain blood cancers. If it succeeds, it could generate sales of $1 billion to $2 billion annually, according to Wall Street analysts, making it among the most lucrative drugs to come from government research.*
>
> *But the government's share of any Kite success would be modest, much lower than some academic research groups have wrangled in immunotherapy deals worth hundreds of millions of dollars.*

As later reported in the story, NIH negotiated a 5% royalty of Kite's sales. The average university royalty rate is 2% according to data from the Association of University Technology Mangers' 2012 annual report on academic licensing. While NIH cannot take an equity in spinout companies as a university could, Kite is not a lab or university spinout. It seems as though NIH/NCI negotiated a good deal. Further, under the law any royalties to the lab must be spent for more research and to reward the inventors so the funds support NCI's mission.

> *Under the second type of contract, known as a cooperative research and development agreement, Kite provides money to the N.C.I. to support research. Kite is now paying $3 million a year to Dr. Rosenberg's lab and has provided $7.5 million to it in total since 2012. Based on its regulatory filings, Kite is paying $7.8 million a year for research agreements and licenses in total, with at least $4 million of that going to the cancer institute and the rest to academic or corporate partners.*
>
> *The taxpayer has invested, too. Dr. Rosenberg estimated that the government has spent roughly $10 million over the years on what has become KTE-C19. He said Kite's $3 million a year is about equal to the taxpayer funding in that area and has helped speed research.*

The government's $10 million funding of this research spans many years, so NCI doubled its research budget for this project only because of the partnership with Kite, a real public benefit.

> *But government officials say few, if any, other companies were interested in the technology at the time Dr. Belldegrun came calling. Dr. Rosenberg said that before Kite, a few companies, including Johnson & Johnson, had looked at an earlier version of his technology but were wary because treatment involved processing each patient's cells.*
>
> *Government-developed technology available to be licensed to companies is posted on the website of the National Institutes of Health. And when the agency intends to grant a license to a particular company, it publishes that in the Federal Register, inviting public comment and possible competing offers. Both steps were taken in the case of Kite, officials said.*

NIH openly advertised that the inventions were available for licensing in December 2010 and they remained available for two years for any company until NIH published a notice on January, 2012 that it intended to award a license to Kite, inviting public comments. One of the hall marks of American entrepreneurship is that small companies like Kite seize opportunities passed over by their larger competitors. If they succeed, good for them. If they fail, they take the hit.

> *Dr. Rosenberg* (NCI researcher) *professes no interest in the business side of the Kite relationship. He does not own stock in any company, even Kite, though he could get up to $150,000 a year in patent royalties if some of Kite's efforts pay off.*

The Federal Technology Transfer Act mandates that federal inventors must receive a portion of royalties received by the lab. If Dr. Rosenberg has indeed made "*among the most lucrative drugs to come from government research*" then God bless him and his team. It's potentially lucrative because it might be a significant breakthrough protecting public health.

> *The N.I.H. does not take equity positions in companies to avoid an appearance of a conflict of interest. So to critics of the government deals, drug prices are crucial to understanding taxpayer value. After all, they ask, is a drug truly widely available — which is what the government says is its measure of success — if it costs too much for some people?*
>
> *Rachel Sachs, an associate law professor at Washington University in St. Louis and expert in innovation policy, said the government had every right to seek price concessions. She noted that the government, through Medicare and Medicaid, was effectively buying its inventions back from itself. "The public is paying for the research*

> *and to the extent that many people, if not most, will pay through public insurance, we're paying again," she said...*
>
> *One mechanism to control pricing already exists. It is called march-in rights, and it lets the N.I.H. take back control of a patent on an invention made with federal funding if the drug is not being made available to the public on reasonable terms. The tool has gone unused.*

How many new products of any kind could meet the test that they don't "cost too much for some people?" Developing new drugs requires lots of time and money, which is why only a handful of countries (primarily in the US) develop them. The public is only paying for early stage research, not the much more costly commercial development. The genius of our system is that we injected patent incentives into public R&D for companies to assume this risk. Our public/private sector partnerships are major drivers of our economy. As stated before, the goal of the law is effective commercialization, not having the government second guess pricing decisions. If Congress wants that, they must amend Bayh-Dole -- and assume responsibility if the system collapses.

Here's how the article ends:

> *Meantime, the relationship between Kite and the National Cancer Institute is expanding to develop treatments for other cancers, including one technique Dr. Rosenberg thinks could be used to attack solid tumors like colon, breast and lung cancer.*
>
> *"The potential for broad applicability is huge," he said.*
>
> *That could mean many lives saved and maybe more billion-dollar drugs for Kite and its investors, with the American taxpayer right in the middle of the deal.*

While it's not unusual to hear citizens sincerely thank those in the military for their service, we should also thank those like Dr. Rosenberg and his colleagues who dedicate their lives to pushing forward the frontiers of science in federal labs and universities. They know that unless their discoveries are commercialized they are not benefitting those they are pledged to serve.

It's too bad that rather than the deserved accolades, NCI and Kite Pharma got a pie in the face from the NY Times. Jonathan Swift said: "When a true genius appears, you can know him by this sign: that all the dunces are in a conspiracy against him." Please don't let the dunces get you down-- keep up the good work. Lives depend on it.

From: Berkley, Dale (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=5EE461C29F5045A49F0ADF82CAAA2F31-BERKLEYD]
Sent: 8/22/2019 3:04:29 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: RE: IMPORTANT FW: 84 FR 39001

b5

Dale D. Berkley, Ph.D., J.D.
Office of the General Counsel, PHD, NIH Branch
Bldg. 31, Rm. 47
Bethesda, MD 20892
301-496-6043
301-402-2528(Fax)

This message is intended for the exclusive use of the recipient(s) named above. It may contain information that is PROTECTED or PRIVILEGED, and it should not be disseminated, distributed, or copied to persons not authorized to receive such information.

From: "kathryn ardizzone" <kathryn.ardizzone@keionline.org>
Date: Wednesday, August 21, 2019 at 10:37:56

To: "Shmilovich, Michael (NIH/NHLBI) [E]" <michael.shmilovich@nih.gov>
Cc: "James Love" <james.love@keionline.org>
Subject: 84 FR 39001

Dear Mr. Shmilovich:

I have now twice asked you a straightforward question: the duration of the license noticed in 84 FR 39001. A responsive answer would be some measure of time, such as "five years," "10 years," or "life of patent." This time, your response is: "the licenses granted to other entities are consistent with the instant contemplated grant of rights to MTTI and I refer you to the responses given by me to your previous inquiries and answers given by my colleagues to your previous inquiries regarding their contemplated licenses."

I have never personally asked you or any of your colleagues about the duration of a prospective license. You and your colleagues have provided vague, hostile replies to my colleagues' inquiries regarding license terms, suggesting a misunderstanding by the NIH regarding your responsibilities in administering the Bayh-Dole Act, which includes an obligation to "promote free competition," (35 USC § 200), among other policy objectives, and to limit the scope of rights for exclusive licenses (35 USC § 209). These provisions of the Bayh-Dole Act are to be implemented on a case by case basis. The NIH is required to publish a new public notice every time there is a new exclusive patent license proposed, and the public is invited to comment on each license, taking into account the specifics of that proposal. The term of the exclusive rights in a license is always a variable that the NIH should justify, and limit when the incentive is excessive.

If NIH's position is that it is not required to disclose to the public the duration of the exclusivity on a taxpayer funded and owned patented invention, then please so state plainly, so that at least the NIH's record of non-transparency is more transparent.

You go on to state: "I do not personally have any licenses on my docket granted for a term shorter than the full patent term and am unaware of any that may have been granted by my colleagues at other Institutes." Taken together, your statements are consistent with the theory that NIH does not engage in the assessment mandated by 209 and routinely grants licenses for life of patent.

35 USC § 209 places mandatory conditions on NIH's authority to enter into an exclusive license agreement. It requires the NIH to engage in an *individualized* assessment, per each prospective license, of whether the scope of rights is no greater than reasonably necessary to incentivize the licensee to bring the technology to market. In the past, NIH granted licenses of 5 to 10 years duration and those agreements succeeded. More importantly, an across-the-board policy of giving full patent rights to prospective licensee without considering the circumstances of a particular license is not consistent with the limits set out in Section 209.

Regarding our questions about royalties, KEI is aware of the confidentiality provisions within Bayh-Dole and the FTTA. Our questions, however, do not implicate those concerns. We did not, for example, request a licensee's "periodic reporting on utilization of the invention," per 35 USC § 209(d)(2).

Moreover, information is confidential only if it is obtained from a person outside the government. *Public Citizen Health Research Group v. National Institutes of Health*, 209 F. Supp. 2d 37, 43 (D.D.C. 2002). KEI's questions did not request information provided by a particular person or corporation outside the government. Rather, KEI asked about *NIH* policy, *NIH* record maintenance, and *NIH* averages/trends. As the recipient of $39 billion annually in taxpayer dollars to fund medical research and development, NIH's royalty policies, recordkeeping systems, and generalized compensation rates for publicly-funded technologies are of legitimate interest to the public, and indeed, in the past, were much more transparent. For example, see Figure 6, page 55 in GAO-18-327, which provides data on the number of licenses issued, by the royalty rate in the license.

The linked image cannot be displayed. The file may have been moved, renamed, or deleted. Verify that the link points to the correct file and location.

Even if the NIH does not provide the royalty rate for specific licenses, you can share data on the licensing guidelines, if any, that are used, (such as those published by the NIH for Start up licenses), and provided data such as that reported in GAO-18-327, but here, in this case, for technologies that are similar to the one being proposed, such as for diagnostic technologies.

Also, we would like to know which databases, if any, the NIH uses to evaluate the adequacy of license royalties. The NIH can refuse to tell us, but if so, please provide some guidance on the limits to the right of the public, who pay federal income taxes and high prices for NIH funded technologies, to have information about the licensing of these taxpayer-funded inventions, in order to provide constructive responses to the Federal Register request for comments.

Finally, can you please point us to the “Licensing Opportunities” notice pertaining to the subject invention? I searched the NIH Office of Intramural Research Office of Technology Transfer Licensing Opportunities website and could not locate a Licensing Opportunity notice issued by the National Heart, Lung and Blood Institute regarding Chemical Conjugates of Evans Blue Derivatives and Their Use as Radiotherapy and Imaging Agents or any “radiotherapeutic against cancers that overexpress integrin αvβ3.”

I look forward to a revised response to my prior inquiries and to your answer to my question about the Licensing Opportunities notice.

Sincerely,

Kathryn Ardizzone, Esq.
Counsel
Knowledge Ecology International
1621 Connecticut Avenue NW, Suite 500
Washington, DC 20009
kathryn.ardizzone@keionline.org
(202) 332-2670

From: Shmilovich, Michael (NIH/NHLBI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7DFE19BFD1D443CEB700B9F22D159A90-SHMILOVM]
Sent: 8/21/2019 2:51:26 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: Fwd: 84 FR 39001

Not sure how to respond to her at this point.

From: "kathryn ardizzone" <kathryn.ardizzone@keionline.org>
Date: Wednesday, August 21, 2019 at 10:37:56
To: "Shmilovich, Michael (NIH/NHLBI) [E]" <michael.shmilovich@nih.gov>
Cc: "James Love" <james.love@keionline.org>
Subject: 84 FR 39001

Dear Mr. Shmilovich:

I have now twice asked you a straightforward question: the duration of the license noticed in 84 FR 39001. A responsive answer would be some measure of time, such as "five years," "10 years," or "life of patent." This time, your response is: "the licenses granted to other entities are consistent with the instant contemplated grant of rights to MTTI and I refer you to the responses given by me to your previous inquiries and answers given by my colleagues to your previous inquiries regarding their contemplated licenses."

I have never personally asked you or any of your colleagues about the duration of a prospective license. You and your colleagues have provided vague, hostile replies to my colleagues' inquiries regarding license terms, suggesting a misunderstanding by the NIH regarding your responsibilities in administering the Bayh-Dole Act, which includes an obligation to "promote free competition," (35 USC § 200), among other policy objectives, and to limit the scope of rights for exclusive licenses (35 USC § 209). These provisions of the Bayh-Dole Act are to be implemented on a case by case basis. The NIH is required to publish a new public notice every time there is a new exclusive patent license proposed, and the public is invited to comment on each license, taking into account the specifics of that proposal. The term of the exclusive rights in a license is always a variable that the NIH should justify, and limit when the incentive is excessive.

If NIH's position is that it is not required to disclose to the public the duration of the exclusivity on a taxpayer funded and owned patented invention, then please so state plainly, so that at least the NIH's record of non-transparency is more transparent.

You go on to state: "I do not personally have any licenses on my docket granted for a term shorter than the full patent term and am unaware of any that may have been granted by my colleagues at other Institutes." Taken together, your statements are consistent with the theory that NIH does not engage in the assessment mandated by 209 and routinely grants licenses for life of patent.

35 USC § 209 places mandatory conditions on NIH's authority to enter into an exclusive license agreement. It requires the NIH to engage in an *individualized* assessment, per each prospective license, of whether the scope of rights is no greater than reasonably necessary to incentivize the licensee to bring the technology to market. In the past, NIH granted licenses of 5 to 10 years duration and those agreements succeeded. More importantly, an across-the-board policy of giving full patent rights to prospective licensee without considering the circumstances of a particular license is not consistent with the limits set out in Section 209.

Regarding our questions about royalties, KEI is aware of the confidentiality provisions within Bayh-Dole and the FTTA. Our questions, however, do not implicate those concerns. We did not, for example, request a licensee's "periodic reporting on utilization of the invention," per 35 USC § 209(d)(2).

Moreover, information is confidential only if it is obtained from a person outside the government. *Public Citizen Health Research Group v. National Institutes of Health*, 209 F. Supp. 2d 37, 43 (D.D.C. 2002). KEI's questions did not request information provided by a particular person or corporation outside the government. Rather, KEI asked about *NIH* policy, *NIH* record maintenance, and *NIH* averages/trends. As the recipient of $39 billion annually in taxpayer dollars to fund medical research and development, NIH's royalty policies, recordkeeping systems, and generalized compensation rates for publicly-funded technologies are of legitimate interest to the public, and indeed, in the past, were much more transparent. For example, see Figure 6, page 55 in GAO-18-327, which provides data on the number of licenses issued, by the royalty rate in the license.

Even if the NIH does not provide the royalty rate for specific licenses, you can share data on the licensing guidelines, if any, that are used, (such as those published by the NIH for Start up licenses), and provided data such as that reported in GAO-18-327, but here, in this case, for technologies that are similar to the one being proposed, such as for diagnostic technologies.

Also, we would like to know which databases, if any, the NIH uses to evaluate the adequacy of license royalties. The NIH can refuse to tell us, but if so, please provide some guidance on the limits to the right of the public, who pay federal income taxes and high prices for NIH funded technologies, to have information about the licensing of these taxpayer-funded inventions, in order to provide constructive responses to the Federal Register request for comments.

Finally, can you please point us to the "Licensing Opportunities" notice pertaining to the subject invention? I searched the NIH Office of Intramural Research Office of Technology Transfer Licensing Opportunities website and could not locate a Licensing Opportunity notice issued by the National Heart, Lung and Blood Institute regarding Chemical Conjugates of Evans Blue Derivatives and Their Use as Radiotherapy and Imaging Agents or any "radiotherapeutic against cancers that overexpress integrin αvβ3."

I look forward to a revised response to my prior inquiries and to your answer to my question about the Licensing Opportunities notice.

Sincerely,

Kathryn Ardizzone, Esq.

Counsel
Knowledge Ecology International
1621 Connecticut Avenue NW, Suite 500
Washington, DC 20009
kathryn.ardizzone@keionline.org
(202) 332-2670

From: Joe Allen [jallen@allen-assoc.com]
Sent: 12/25/2016 8:35:01 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]
Subject: Final version
Attachments: The National Cancer Institute Didn't Deserve Its Treatment in the NY Times.docx

Got some uninterupted time to hone this down. If you have a minute, please look it over and see if you find any factual mistakes and I'll shoot if off to Gene to see when he wants to run it.

Thanks!

--

Joseph P. Allen
President
Allen and Associates
60704 Rt. 26, South
Bethesda, OH 43719
(W) 740-484-1814
(c) b6
www.allen-assoc.com

The National Cancer Institute Doesn't Deserve This Treatment From the New York Times

By Joseph P. Allen

Imagine that you found a drug at a government lab that others passed over which promises to cure, not just treat, certain blood cancers. You entered into a cooperative R&D agreement which doubled the lab's budget in a critical research area while they leverage the expertise of your company. You're a small company taking on the big boys, with a state of the art facility in the U.S. hoping to be first to market with a revolutionary therapy.

Now imagine you're a researcher at the National Cancer Institute (NCI, part of the National Institutes of Health) working on what could be a breakthrough in the fight against cancer. But it will never help desperate patients without a commercial partner. Suddenly there's a new company that shares your vision, with a co-founder who spent time at NCI and deeply respects your research team. They raise millions of dollars for critical clinical trials required to develop a useable drug. You've negotiated an agreement securing funding for research you couldn't perform otherwise. If the invention is successful the lab will receive millions of dollars for research, but most importantly, many lives that would have been lost will be saved.

This may sound like a dream come true. But anyone reading the New York Times article "Harnessing the U.S. Taxpayer to Fight Cancer and Make Profits" (http://www.nytimes.com/2016/12/19/health/harnessing-the-us-taxpayer-to-fight-cancer-and-make-profits.html?action=click&contentCollection=health&region=rank&module=package&version=highlights&contentPlacement=2&pgtype=sectionfront) can be excused for thinking the public has been cheated.

The NY Times has been on quite a roll lately (no, not talking about the letter from the Publisher/Executive Editor (http://www.nytimes.com/2016/11/13/us/elections/to-our-readers-from-the-publisher-and-executive-editor.html?_r=0) apologizing for its biased election coverage). A week before the NCI story, they ran "Lives and Profits in the Balance: The High Stakes of Medical Patents" (http://www.nytimes.com/2016/12/11/us/retro-report-medical-patents-profits.html) repeating the myth that the government is failing to use the authorities of the Bayh-Dole Act to control drug prices. That's also a theme of the NCI story.

These articles are part of the campaign pressuring NIH into misusing the Bayh-Dole Act for compulsory licenses against drugs deemed too expensive. So let's examine the story's criticisms of the partnership between Kite Pharma and NCI to commercialize a promising immunotherapy discovery.

> *Kite's treatment, a form of immunotherapy called CAR-T, was initially developed by a team of researchers at the National Cancer Institute...*

Not only wasn't the drug "developed" by NCI-- it's not developed. NCI followed their 2009 discovery with mouse tests, a single patient study and data from a clinical study of eight people. That's far from development. Because of Kite's financial backing the drug is in Phase I testing (http://kitepharma.com/pipeline/). The odds of any drug going from there to the marketplace are about 10% (http://www.reuters.com/article/us-pharmaceuticals-success-idUSTRE71D2U920110214). This is the stage where the costs-- and risks-- of drug development increase exponentially. This burden falls on Kite. The other drugs being developed in the partnership are not even in Phase I yet.

> *Kite's first drug, called KTE-C19, could help thousands of patients each year in the United States with certain blood cancers. If it succeeds, it could generate sales of $1 billion to $2 billion annually, according to Wall Street analysts, making it among the most lucrative drugs to come from government research.*

It "could generate sales of $1 billion to $2 billion annually"-- or it could generate nothing. It's too early to know if it's "among the most lucrative drugs to come from government research" or another promising drug that dies in clinical trials. When drug trials backed by small companies fail, people lose their jobs, investors lose their money and the business goes under. While we don't know the result yet, we do know that without companies like Kite these government-funded discoveries would never get out of the lab.

> *Defenders say that the partnership will likely bring a lifesaving treatment to patients, something the government cannot really do by itself, and that that is what matters most.*
>
> *Critics say that taxpayers will end up paying twice for the same drug — once to support its development and a second time to buy it — while the company reaps the financial benefit.*
>
> *"If this was not a government-funded cancer treatment — if it was for a new solar technology, for example — it would be scandalous to think that some private investors are reaping massive profits off a taxpayer-funded invention," said James Love, director of Knowledge Ecology International, an advocacy group concerned with access to medicines.*

It's a myth that the government is developing drugs. Federally funded inventions are early stage discoveries, far removed from being useful products. The risks and expense of commercial development fall on the private sector. Drug development often costs hundreds of millions to billions of dollars with a huge failure rate. It was the concern that potentially important medical discoveries were wasting away that led Congress to enact the Bayh-Dole Act creating incentives for industry to partner with universities and federal labs so these discoveries could benefit taxpayers. They are not "paying twice for the same drugs" but finally have a system transforming publicly funded research into new products, jobs and companies benefitting the nation. It's also given the U.S. undisputed leadership in the life sciences.

> *The debate goes squarely to one of the nation's most vexing challenges: rising health care and drug prices. Kite is one of a growing number of drug and biotech companies relying on federal laboratories. Analysts expect the company to charge at least $200,000 for the new treatment, which is intended as a one-time therapy for patients.*
>
> *While the law allows the government to demand drug-price concessions from its private-sector partners, the government has declined to do so with Kite and generally disdains the practice.*

Bayh-Dole only allows agencies to "march-in" requiring compulsory licenses if good faith efforts are not being made to commercialize a federally funded invention or if the licensee cannot produce enough product to meet a national security or health emergency (see NIH Director Collins Stands Up to the March in Mob (http://www.ipwatchdog.com/2016/06/27/nih-director-collins-march-in-mob/id=70391/ and When Government Tried March In Rights to Control Health Care Costs (http://www.ipwatchdog.com/2016/05/02/march-in-rights-health-care-costs/id=68816/). Regardless, persistent efforts are underway to pressure NIH into misapplying the law. That appears to be a goal of this story.

> *Insisting on lower prices, federal researchers say, would drive away innovative partners that speed the drug-development process and benefit patients. But with the government doing so much pivotal research, others say that the private sector cannot afford to walk away.*
>
> *"The market is so reliant on the knowledge and know-how that comes out of the government and academic labs," said Dr. Aaron Kesselheim, director of the Program on Regulation, Therapeutics and Law at Brigham & Women's Hospital in Boston. Price curbs, he said, "would not suddenly lead to a total abandonment of this pipeline. It couldn't possibly."*
>
> *Drug makers would be especially unlikely to turn away from immunotherapy, where the promising science has set off a "gold rush mentality," according to Mark Edwards of Bioscience Advisors, a company which tracks pharmaceutical licensing deals.*

But companies did turn away when this was tried before. In 1989 NIH was pressured by critics into including "reasonable pricing" language in its Cooperative R&D Agreements (CRADAS). The result-- partnerships collapsed and the policy had to be rescinded (https://www.ott.nih.gov/policies-reports). Thinking that because industry sees universities and federal labs as valuable research partners means that we can pull the rug out from under them because they have nowhere else to go is short sighted. China is targeting the life sciences, pouring billions into their research universities to challenge our lead. They would welcome U.S. biotech and drug companies willing to move research there with open arms. They could also pull their own bait and switch after pumping our companies of their expertise.

> *Kite's first drug, called KTE-C19, could help thousands of patients each year in the United States with certain blood cancers. If it succeeds, it could generate sales of $1 billion to $2 billion annually, according to Wall Street analysts, making it among the most lucrative drugs to come from government research.*
>
> *But the government's share of any Kite success would be modest, much lower than some academic research groups have wrangled in immunotherapy deals worth hundreds of millions of dollars.*

NIH negotiated a 5% royalty of Kite's sales. The average university royalty rate is 2% according to data from the Association of University Technology Mangers' 2012 report on academic licensing. NIH cannot take an equity like a university on spinout companies, but that's irrelevant-- Kite isn't a spinout. It seems like NCI negotiated a good deal. Under the law royalties must be spent on more research and to reward their inventors so these funds support NCI's mission.

> *Under the second type of contract, known as a cooperative research and development agreement, Kite provides money to the N.C.I. to support research. Kite is now paying $3 million a year to Dr. Rosenberg's lab and has provided $7.5 million to it in total since 2012. Based on its regulatory filings, Kite is paying $7.8 million a year for research agreements and licenses in total, with at least $4 million of that going to the cancer institute and the rest to academic or corporate partners.*
>
> *The taxpayer has invested, too. Dr. Rosenberg estimated that the government has spent roughly $10 million over the years on what has become KTE-C19. He said Kite's $3 million a year is about equal to the taxpayer funding in that area and has helped speed research.*

The government's $10 million funding spans many years. Because of just four years of partnership with Kite, NCI significantly increased its research in a critical area of public health.

> *But government officials say few, if any, other companies were interested in the technology at the time Dr. Belldegrun came calling. Dr. Rosenberg said that before Kite, a few companies, including Johnson & Johnson, had looked at an earlier version of his technology but were wary because treatment involved processing each patient's cells.*

> *Government-developed technology available to be licensed to companies is posted on the website of the National Institutes of Health. And when the agency intends to grant a license to a particular company, it publishes that in the Federal Register, inviting public comment and possible competing offers. Both steps were taken in the case of Kite, officials said.*

In December, 2010 NIH advertised their inventions were available for licensing. They remained so for two years. NIH published a notice in January, 2012 that it intended to award a license to Kite, inviting public comments. The process was open and fair. One of the hallmarks of American entrepreneurship is that small companies like Kite seize opportunities missed by larger competitors. If they succeed, good for them. If they fail, they take the hit.

> *Dr. Rosenberg* (NCI researcher) *professes no interest in the business side of the Kite relationship. He does not own stock in any company, even Kite, though he could get up to $150,000 a year in patent royalties if some of Kite's efforts pay off.*

Federal law mandates that agencies must share royalties with their inventors when patents are licensed. If Dr. Rosenberg made "*among the most lucrative drugs to come from government research*" then God bless him and his team. It's potentially lucrative because it might be a significant breakthrough protecting public health. It also might fail.

> *The N.I.H. does not take equity positions in companies to avoid an appearance of a conflict of interest. So to critics of the government deals, drug prices are crucial to understanding taxpayer value. After all, they ask, is a drug truly widely available — which is what the government says is its measure of success — if it costs too much for some people?*
>
> *Rachel Sachs, an associate law professor at Washington University in St. Louis and expert in innovation policy, said the government had every right to seek price concessions. She noted that the government, through Medicare and Medicaid, was effectively buying its inventions back from itself. "The public is paying for the research and to the extent that many people, if not most, will pay through public insurance, we're paying again," she said...*
>
> *One mechanism to control pricing already exists. It is called march-in rights, and it lets the N.I.H. take back control of a patent on an invention made with federal funding if the drug is not being made available to the public on reasonable terms. The tool has gone unused.*

How many new products of any kind could meet the test that they don't "cost too much for some people?" Developing new drugs requires lots of time and money with daunting odds against success, which is why only a handful of countries (primarily the US) develop them. The public is only paying for early stage research, not for costly commercial development. The genius of our system is that we injected patent incentives into public R&D so companies will assume this risk. When they fail, the company, not the taxpayer, foots the bill. The goal of the Bayh-Dole Act is commercialization, not having the government second guess pricing decisions. If Congress wants that, they must amend the law -- and assume responsibility if the system collapses.

> *Meantime, the relationship between Kite and the National Cancer Institute is expanding to develop treatments for other cancers, including one technique Dr. Rosenberg thinks could be used to attack solid tumors like colon, breast and lung cancer.*
>
> *"The potential for broad applicability is huge," he said.*
>
> *That could mean many lives saved and maybe more billion-dollar drugs for Kite and its investors, with the American taxpayer right in the middle of the deal.*

While it's not unusual to hear citizens thank those in the military for their service, we should also thank researchers like Dr. Rosenberg and his colleagues who dedicate their lives to alleviating human suffering. But that can only happen when their discoveries are commercialized; otherwise they are merely generating interesting research papers.

Rather than the deserved accolades, NCI and Kite Pharma got a pie in the face from the NY Times. Perhaps they'll feel better recalling the words of Jonathan Swift: "When a true genius appears, you can know him by this sign: that all the dunces are in a conspiracy against him." Don't let the dunces get you down-- keep up the good work. Lives depend on it.

From: Shmilovich, Michael (NIH/NHLBI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7DFE19BFD1D443CEB700B9F22D159A90-SHMILOVM]
Sent: 8/20/2019 4:16:19 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: FW: 84 FR 39001

How now Horatio?

From: kathryn ardizzone <kathryn.ardizzone@keionline.org>
Sent: Tuesday, August 20, 2019 12:13
To: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>
Cc: James Love <james.love@keionline.org>
Subject: Re: 84 FR 39001

Dear Mr. Shmilovich:

Thank you for your reply. Please clarify your response to Question No. 2. Your answer, to a question regarding a specific licensing decision, was that "[t]his question has been addressed multiple times through [my] prior inquiries." However, this was the first time that I, or anyone at KEI, asked you about the terms of this prospective license, to MTTI Technologies, referenced in 84 FR 39001. If the NIH's position is that KEI is not entitled to know, and the NIH is not required to disclose, the contemplated terms of the proposed license, then please so state.

In addition, please answer these follow-up questions:

1. How will the NIH determine that the proposed royalty for the prospective license is appropriate compensation for the federally-owned technology?
    a. Does the NIH have a set of royalty guidelines?
    b. Does the NIH have a database of royalty rates on federally licensed technology? If so, what is the name of the database and where is it managed?
    c. Does the NIH have access to databases of royalty rates from third parties? If so, which databases does the NIH use?
    d. For comparable licenses, what was the average/typical royalty rate?
2. Are you aware of any NIH exclusive licenses for which the term of the license is shorter than the term of the patent? And if so, can you provide information to identify the licenses?

Thank you for your consideration.

Sincerely,

Kathryn Ardizzone

On Tue, Aug 20, 2019 at 10:49 AM Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov> wrote:

> Dear Ms. Ardizzone:

1. The stage of development of the licensed technology (what clinical trials and research and development has been performed);

Preclinical/Early stage

2. What the term of the license would be (i.e., life of patent, or fewer years than that).

This question has been addressed multiple times through your prior inquiries and has not changed.

Regards,

Michael A. Shmilovich, Esq., CLP

NIH National Heart, Lung, and Blood Institute
Office of Technology Transfer and Development
31 Center Drive Room 4A29, MSC2479
Bethesda, MD 20892-2479
o. 301.435.5019

shmilovm@nih.gov

This message may contain privileged and confidential information intended only for the use of the individual(s) or entity named above. If you are not the intended recipient, you are hereby notified that any use, dissemination, distribution, or copying of this message or its content is strictly prohibited. If you have received this message in error, please notify sender immediately and destroy the message without making a copy. Thank you.

From: kathryn ardizzone <kathryn.ardizzone@keionline.org>
Sent: Tuesday, August 20, 2019 09:55
To: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>
Cc: James Love <james.love@keionline.org>
Subject: 84 FR 39001

Dear Mr. Shmilovich:

Regarding the prospective license noticed in 84 FR 39001, can you please tell me:

1. The stage of development of the licensed technology (what clinical trials and research and development has been performed); and

2. What the term of the license would be (i.e., life of patent, or fewer years than that).

Thank you,

Kathryn Ardizzone, Esq.

Counsel

Knowledge Ecology International

1621 Connecticut Avenue NW, Suite 500

Washington, DC 20009

kathryn.ardizzone@keionline.org

(202) 332-2670

--
Kathryn Ardizzone, Esq.
Counsel
Knowledge Ecology International
1621 Connecticut Avenue NW, Suite 500
Washington, DC 20009
kathryn.ardizzone@keionline.org
(202) 332-2670

From: Shmilovich, Michael (NIH/NHLBI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7DFE19BFD1D443CEB700B9F22D159A90-SHMILOVM]
Sent: 8/20/2019 2:16:26 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: FW: 84 FR 39001

Mark – should I bother responding?

From: kathryn ardizzone <kathryn.ardizzone@keionline.org>
Sent: Tuesday, August 20, 2019 09:55
To: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>
Cc: James Love <james.love@keionline.org>
Subject: 84 FR 39001

Dear Mr. Shmilov:

Regarding the prospective license noticed in 84 FR 39001, can you please tell me:

1. The stage of development of the licensed technology (what clinical trials and research and development has been performed); and
2. What the term of the license would be (i.e., life of patent, or fewer years than that).

Thank you,

Kathryn Ardizzone, Esq.
Counsel
Knowledge Ecology International
1621 Connecticut Avenue NW, Suite 500
Washington, DC 20009
kathryn.ardizzone@keionline.org
(202) 332-2670

From: Plude, Denise (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/CN=RECIPIENTS/CN=PARKSDE]
Sent: 12/2/2016 1:42:49 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]
Subject: FW: Final Draft for #350339
Attachments: NIH Draft Response AS750330 & S750353 Paul Davis.docx

Let me know if I should alert Exec Sec to any concerns.

From: Whitfield, Michelle D. (NIH/OD) [E]
Sent: Friday, December 02, 2016 8:41 AM
To: Plude, Denise (NIH/OD) [E] <pludede@mail.nih.gov>
Subject: Final Draft for #350339
Importance: High

Good morning Denise,

I just sent #350339 to OSP as an FYI in DDRMS, but I thought I would e-mail it to you also. I am attaching the draft final response that Dr. Hudson will sign/send. OS has cleared this draft. If OSP has any concerns regarding this draft, please let me know by 11:00 am today, Dec. 2.

Thank you,
Michelle

Paul Davis
Knowledge Ecology International
1621 Connecticut Avenue, Suite 500
Washington, DC 20009

Dear Mr. Davis:

Thank you for your October 17 and October 26, 2016, e-mails to the Secretary of Health and Human Services, Sylvia Burwell. Secretary Burwell has asked that I respond on her behalf.

This letter is to clarify the position of the National Institutes of Health (NIH) concerning the use of government authorities to address the issues you raised regarding Xtandi®. In a June 20, 2016 letter from Dr. Francis Collins, Director of the NIH, to Andrew Goldman, Knowledge Ecology International, the NIH declined to use the government's march-in authorities found at 35 U.S.C. §203 or to exercise the government's non-exclusive royalty-free government use license for Xtandi® (enzalutamide). The NIH has no additional information at this time that would compel it to reverse this decision

In addition, I was able to meet with your colleagues James Love, Andrew Goldman, and Zach Struver at our meeting on November 7, 2016. Thank you again for coming to NIH and providing more information about your concern about barriers to drug access for patients in middle- and lower-income countries.

Please share this response with the organizations that signed the October 17, 2016, e-mail to Secretary Burwell.

Sincerely,

Kathy Hudson, Ph.D.
Deputy Director for Science, Outreach and Policy

From: Amar, Anna (NIH/NCI) [E] [/O=NIH/OU=NIHEXCHANGE/CN=NIAID/CN=AAMAR]
Sent: 1/3/2017 5:32:37 PM
To: Lambert, Richard (NIH/NIAID) [C] [/O=NIH/OU=NIHEXCHANGE/cn=NIAID/cn=LAMBERTR]; Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]; Mowatt, Michael (NIH/NIAID) [E] [/O=NIH/OU=NIHEXCHANGE/cn=NIAID/cn=MMOWATT]
Subject: RE: [Ip-health] NIH grant for "Development of an Intellectual Property (IP) Strategy for the Commercial Advancement of a Direct Phase II SBIR-Funded technology

That doesn't make any sense!

How can we get some educational information out there so those who are not aware can be better informed?

-----Original Message-----
From: Lambert, Richard (NIH/NIAID) [C]
Sent: Tuesday, January 03, 2017 12:30 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>; Mowatt, Michael (NIH/NIAID) [E] <MMOWATT@niaid.nih.gov>; Amar, Anna (NIH/NCI) [E] <anna.amar@nih.gov>
Subject: FW: [Ip-health] NIH grant for "Development of an Intellectual Property (IP) Strategy for the Commercial Advancement of a Direct Phase II SBIR-Funded technology

Another FYI

Richard A. Lambert
Contractor
National Institute of Allergy and Infectious Diseases National Institutes of Health U.S. Department of Health and Human Services
5601 Fishers Lane, Rm. 2G47, MSC 9804
Bethesda, MD 20892-9804
(Courier: Rockville, MD. 20852)
301.496.2644 main officeline
240.627.3706 direct line
FAX 240.627.3117
lambertr@niaid.nih.gov
This message is intended for the exclusive use of the recipient(s) identified above. The information in this email and any of its attachments may be confidential and/or sensitive and should not be retained, disseminated, distributed or copied by or to persons not authorized to receive such information. If you receive this message in error please inform the sender and delete it immediately from your mailbox or any other storage devices. The National Institute of Allergy and Infectious Diseases (NIAID) shall not accept liability for any unauthorized statements made by the sender in this message.

-----Original Message-----
From: Michael H Davis [mailto:m.davis@csuohio.edu]
Sent: Tuesday, January 03, 2017 12:17 PM
To: Jamie Love <james.love@keionline.org>; Ip-health <ip-health@lists.keionline.org>
Subject: Re: [Ip-health] NIH grant for "Development of an Intellectual Property (IP) Strategy for the Commercial Advancement of a Direct Phase II SBIR-Funded technology

They won't march in because they don't know anything about prices but they know all about intellectual property? Is this agency out of its mind?

Sent from my T-Mobile 4G LTE Device

-------- Original message --------
From: Jamie Love <james.love@keionline.org>
Date: 1/3/17 12:03 PM (GMT-05:00)
To: Ip-health <ip-health@lists.keionline.org>
Subject: [Ip-health] NIH grant for "Development of an Intellectual Property (IP) Strategy for the Commercial Advancement of a Direct Phase II SBIR-Funded technology

https://projectreporter.nih.gov/project_info_description.cfm?aid=9253581&icde=32443948

Apparently the NIH will give you a grant to help you patent the heck out of a technology where they are also funding the research.

Project Number: 1SB1HL137591-01
Former Number: 2SB1HL131050-03

Contact PI / Project Leader: KARLSSON, SVEN M

Title: DEVELOPMENT OF AN INTELLECTUAL PROPERTY (IP) STRATEGY FOR THE COMMERCIAL ADVANCEMENT OF A DIRECT PHASE II SBIR-FUNDED HUMAN PLATELET BIOREACTOR Awardee Organization: PLATELET BIOGENESIS, INC.

PROJECT SUMMARY/ABSTRACT

Platelet BioGenesis is developing a microfluidic bioreactor to produce human platelets at clinical scale. Platelets are the 'band-aids' of the bloodstream, responsible for clot formation and blood vessel repair. Low platelet count is a significant consequence of cancer treatment, transplant, and surgery, for which plate- lets are a critical first-line therapy to prevent mortality due to uncontrolled bleeding. Platelets are
de- rived exclusively from volunteer donors. Risk of bacterial growth during room temperature storage limits plate- let shelf life to 5 days, 2 of which are expended by bacterial screening, and 1 during transport to hospitals. As a result blood centers typically do not have more than a 1.5-day platelet inventory available for transfu- sion, making platelet unit inventory especially vulnerable to routine depletion[1, 2]. To address this ma- jor unmet need we are developing a platelet bioreactor that reproduces key features of adult bone marrow (physiological
microenvironment) to trigger platelet production from human induced pluripotent stem cells (hiP- SCs, a replenishable source of progenitor cells which can be stored frozen for years) at clinical/commercial scale.
This SBIR CRP Program proposal for Technical Assistance (SB1) outlines a comprehensive intellectual property strategy for Platelet BioGenesis to develop a proprietary, patent protected technology to produce cGMP-compliant human bioreactor-derived platelets at commercial scale for clinical use in 3 specific aims: Aim 1. Understanding the Patent Landscape.
We will work with IP counsel to: (1) identify and assess licens- ing various third party patents and patent applications related to megakaryocyte differentiation protocols and the platelet bioreactor, (2) perform further patent searches (landscape and/or freedom to operate) to ensure that we are able to commercialize our technology without infringement, and/or (3) identify any additional third party patents that may be licensed by us to further improve our competitive commercial position. Aim 2. Protecting Proprietary Technology to Enable Commercialization. We will work with IP counsel to identify intellectual property generated by us and will formulate a strategy for protecting such intellectual prop- erty, either by filing patent applications or ensuring that the technology is maintained as a trade secret. Aim 3. IP Agreements.
We will work with the IP counsel to: (1) review our non-disclosure agreements, em- ployment or consultant agreements to ensure the ownership and protection of our intellectual property, and (2) negotiate and enter into license agreements with cGMP-compliant hiPSC suppliers for access to relevant cell lines. cGMP-hiPSC line master banks will be maintained and differentiated into megakaryocytes under established supply agreements using proprietary cell culture protocols.

Public Health Relevance Statement:

PROJECT NARRATIVE Human platelets are presently derived exclusively from volunteer donors and have a shelf life of 5 days, mak- ing platelet unit inventory sensitive to depletion and putting platelet recipients at risk of sepsis and viruses dur- ing surgery, pregnancy and birth, cancer/HIV/burn-treatment, and transplant. There are currently no licensed therapeutics that immediately increase platelet counts, and insufficient platelet supply to meet projected US demand (~2.3M platelet units/year in 2013). Platelet BioGenesis has: identified cGMP-compliant hiPSC lines, validated megakaryocyte differentiation protocol and platelet storage-permissive media, and established a mi- crofluidic bioreactor to rapidly trigger functional platelet production at clinical/commercial scale. We now seek to develop a comprehensive IP strategy for linking these key technologies, which is necessary to advance bio- reactor-derived platelets (bdPLTs) for clinical use.

--
James Love. Knowledge Ecology International http://www.keionline.org/donate.html
KEI DC tel: +1.202.332.2670, US Mobile: +1.202.361.3040, Geneva Mobile: +41.76.413.6584, twitter.com/jamie_love

---

Ip-health mailing list
Ip-health@lists.keionline.org
http://lists.keionline.org/mailman/listinfo/ip-health_lists.keionline.org

---

Ip-health mailing list
Ip-health@lists.keionline.org
http://lists.keionline.org/mailman/listinfo/ip-health_lists.keionline.org

From: Myles, Renate (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7D317F5626934585B3692A1823C1B522-MYLESR]
Sent: 7/31/2019 8:03:07 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
CC: Fine, Amanda (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=61290b74aa9a44358954c45439ffdeb6-fineab]; Wojtowicz, Emma (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=45c6610aca6e44a08d497630425e5ecd-wojtowiczem]
Subject: FW: NIH licensing

Please review:

b5

From: Myles, Renate (NIH/OD) [E]
Sent: Wednesday, July 31, 2019 3:40 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>; Hallett, Adrienne (NIH/OD) [E] <adrienne.hallett@nih.gov>; Berkson, Laura (NIH/OD) [E] <laura.berkson@nih.gov>
Cc: Fine, Amanda (NIH/OD) [E] <amanda.fine@nih.gov>; Wojtowicz, Emma (NIH/OD) [E] <emma.wojtowicz@nih.gov>
Subject: RE: NIH licensing

Hi Mark:

The letter looks good to me.

b5

Thanks,

Renate

From: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Sent: Wednesday, July 31, 2019 2:55 PM
To: Hallett, Adrienne (NIH/OD) [E] <adrienne.hallett@nih.gov>; Myles, Renate (NIH/OD) [E] <mylesr@mail.nih.gov>; Berkson, Laura (NIH/OD) [E] <laura.berkson@nih.gov>
Cc: Fine, Amanda (NIH/OD) [E] <amanda.fine@nih.gov>; Wojtowicz, Emma (NIH/OD) [E] <emma.wojtowicz@nih.gov>
Subject: RE: NIH licensing

Unless you have comments, this should be final. Could you review it please before I send it out?

From: Hallett, Adrienne (NIH/OD) [E] <adrienne.hallett@nih.gov>
Sent: Wednesday, July 31, 2019 9:27 AM
To: Myles, Renate (NIH/OD) [E] <mylesr@mail.nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Berkson, Laura (NIH/OD) [E] <laura.berkson@nih.gov>
Cc: Fine, Amanda (NIH/OD) [E] <amanda.fine@nih.gov>; Wojtowicz, Emma (NIH/OD) [E] <emma.wojtowicz@nih.gov>
Subject: RE: NIH licensing

Okay by me.

From: Myles, Renate (NIH/OD) [E] <mylesr@mail.nih.gov>
Sent: Wednesday, July 31, 2019 9:00 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Hallett, Adrienne (NIH/OD) [E] <adrienne.hallett@nih.gov>; Berkson, Laura (NIH/OD) [E] <laura.berkson@nih.gov>
Cc: Fine, Amanda (NIH/OD) [E] <amanda.fine@nih.gov>; Wojtowicz, Emma (NIH/OD) [E] <emma.wojtowicz@nih.gov>
Subject: FW: NIH licensing

Hi Mark, Adrienne and Laura:

Can we respond to the reporter about the letter to FC since we've responded already on this topic? b5

b5

b5

From: Andrew Siddons <andrewsiddons@cqrollcall.com>
Sent: Wednesday, July 31, 2019 8:00 AM
To: Myles, Renate (NIH/OD) [E] <mylesr@mail.nih.gov>
Subject: NIH licensing

Hi Renate -- I hope all is well. As you are probably aware a few advocacy groups are calling attention to the NIH's licensing practices and asking for more transparency and more consideration of pricing when granting licenses... I'm referring specifically to the letter KEI sent last week (link below) and the letter that Patients for Affordable Drugs sent Tuesday (attached). Additionally, Senators Van Hollen and Scott are planning to introduce a bill related to drugs that benefit from NIH research, so I'm trying to write a story about this broader issue.

I know you can't comment on pending legislation but maybe you could comment more broadly with the NIH's position on licensing, prices and access. It woudl be great to get a response by early this afternoon. Thanks!

https://www.keionline.org/wp-content/uploads/KEI_Letter_HouseOversightCommittee_-NIH_Lack_of_Transparency_22July2019.pdf

Andrew Siddons
CQ Roll Call
Office: 202-650-6441
Mobile: b6

From: Lambert, Richard (NIH/NIAID) [C] [/O=NIH/OU=NIHEXCHANGE/CN=NIAID/CN=LAMBERTR]
Sent: 1/3/2017 5:32:16 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]
Subject: FW: [Ip-health] NIH grant for "Development of an Intellectual Property (IP) Strategy for the Commercial Advancement of a Direct Phase II SBIR-Funded technology

Richard A. Lambert
Contractor
National Institute of Allergy and Infectious Diseases
National Institutes of Health
U.S. Department of Health and Human Services
5601 Fishers Lane, Rm. 2G47, MSC 9804
Bethesda, MD 20892-9804
(Courier: Rockville, MD. 20852)
301.496.2644 main officeline
240.627.3706 direct line
FAX 240.627.3117
lambertr@niaid.nih.gov
This message is intended for the exclusive use of the recipient(s) identified above. The information in this email and any of its attachments may be confidential and/or sensitive and should not be retained, disseminated, distributed or copied by or to persons not authorized to receive such information. If you receive this message in error please inform the sender and delete it immediately from your mailbox or any other storage devices. The National Institute of Allergy and Infectious Diseases (NIAID) shall not accept liability for any unauthorized statements made by the sender in this message.

-----Original Message-----
From: Michael H Davis [mailto:m.davis@csuohio.edu]
Sent: Tuesday, January 03, 2017 12:28 PM
To: Jamie Love <james.love@keionline.org>; Ip-health <ip-health@lists.keionline.org>
Subject: Re: [Ip-health] NIH grant for "Development of an Intellectual Property (IP) Strategy for the Commercial Advancement of a Direct Phase II SBIR-Funded technology

Get this. If you read clearly you'll see this is not just about patent, which in theory promotes progress by publishing the patent to the world. No, they say they will advise the fundee on keeping this publicly funded research a trade secret! How that promotes progress is rather difficult to discover. This it's agency capture at its very worst

Sent from my T-Mobile 4G LTE Device

-------- Original message --------
From: Jamie Love <james.love@keionline.org>
Date: 1/3/17 12:03 PM (GMT-05:00)
To: Ip-health <ip-health@lists.keionline.org>
Subject: [Ip-health] NIH grant for "Development of an Intellectual Property (IP) Strategy for the Commercial Advancement of a Direct Phase II SBIR-Funded technology

https://projectreporter.nih.gov/project_info_description.cfm?aid=9253581&icde=32443948

Apparently the NIH will give you a grant to help you patent the heck out of a technology where they are also funding the research.

Project Number: 1SB1HL137591-01
Former Number: 2SB1HL131050-03
Contact PI / Project Leader: KARLSSON, SVEN M

Title: DEVELOPMENT OF AN INTELLECTUAL PROPERTY (IP) STRATEGY FOR THE COMMERCIAL ADVANCEMENT OF A DIRECT PHASE II SBIR-FUNDED HUMAN PLATELET BIOREACTOR Awardee Organization: PLATELET BIOGENESIS, INC.

PROJECT SUMMARY/ABSTRACT

Platelet BioGenesis is developing a microfluidic bioreactor to produce human platelets at clinical scale. Platelets are the 'band-aids' of the bloodstream, responsible for clot formation and blood vessel repair. Low platelet count is a significant consequence of cancer treatment, transplant, and surgery, for which plate- lets are a critical first-line therapy to prevent mortality due to uncontrolled bleeding. Platelets are de- rived exclusively from volunteer donors. Risk of bacterial growth during room temperature storage limits plate- let shelf life to 5 days, 2 of which are expended by bacterial screening, and 1 during transport to hospitals. As a result blood centers typically do not have more than a 1.5-day platelet inventory available for transfu- sion, making platelet unit inventory especially vulnerable to routine depletion[1, 2]. To address this ma- jor unmet need we are developing a platelet bioreactor that reproduces key features of adult bone marrow (physiological microenvironment) to trigger platelet production from human induced pluripotent stem cells (hiP- SCs, a replenishable source of progenitor cells which can be stored frozen for years) at clinical/commercial scale.

This SBIR CRP Program proposal for Technical Assistance (SB1) outlines a comprehensive intellectual property strategy for Platelet BioGenesis to develop a proprietary, patent protected technology to produce cGMP-compliant human bioreactor-derived platelets at commercial scale for clinical use in 3 specific aims: Aim 1. Understanding the Patent Landscape.

We will work with IP counsel to: (1) identify and assess licens- ing various third party patents and patent applications related to megakaryocyte differentiation protocols and the platelet bioreactor, (2) perform further patent searches (landscape and/or freedom to operate) to ensure that we are able to commercialize our technology without infringement, and/or (3) identify any additional third party patents that may be licensed by us to further improve our competitive commercial position. Aim 2. Protecting Proprietary Technology to Enable Commercialization. We will work with IP counsel to identify intellectual property generated by us and will formulate a strategy for protecting such intellectual prop- erty, either by filing patent applications or ensuring that the technology is maintained as a trade secret. Aim 3. IP Agreements.

We will work with the IP counsel to: (1) review our non-disclosure agreements, em- ployment or consultant agreements to ensure the ownership and protection of our intellectual property, and (2) negotiate and enter into license agreements with cGMP-compliant hiPSC suppliers for access to relevant cell lines. cGMP-hiPSC line master banks will be maintained and differentiated into megakaryocytes under estab- lished supply agreements using proprietary cell culture protocols.

Public Health Relevance Statement:

PROJECT NARRATIVE Human platelets are presently derived exclusively from volunteer donors and have a shelf life of 5 days, mak- ing platelet unit inventory sensitive to depletion and putting platelet recipients at risk of sepsis and viruses dur- ing surgery, pregnancy and birth, cancer/HIV/burn-treatment, and transplant. There are currently no licensed therapeutics that immediately increase platelet counts, and insufficient platelet supply to meet projected US demand (~2.3M platelet units/year in 2013). Platelet BioGenesis has: identified cGMP-compliant hiPSC lines, validated megakaryocyte differentiation protocol and platelet storage-permissive media, and established a mi- crofluidic bioreactor to rapidly trigger functional platelet production at clinical/commercial scale. We now seek to develop a comprehensive IP strategy for linking these key technologies, which is necessary to advance bio- reactor-derived platelets (bdPLTs) for clinical use.

--
James Love. Knowledge Ecology International http://www.keionline.org/donate.html
KEI DC tel: +1.202.332.2670, US Mobile: +1.202.361.3040, Geneva Mobile:
+41.76.413.6584, twitter.com/jamie_love

Ip-health mailing list
Ip-health@lists.keionline.org
http://lists.keionline.org/mailman/listinfo/ip-health_lists.keionline.org

---

Ip-health mailing list
Ip-health@lists.keionline.org
http://lists.keionline.org/mailman/listinfo/ip-health_lists.keionline.org

From: Myles, Renate (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7D317F5626934585B3692A1823C1B522-MYLESR]
Sent: 7/31/2019 8:08:49 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
CC: Fine, Amanda (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=61290b74aa9a44358954c45439ffdeb6-fineab]; Wojtowicz, Emma (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=45c6610aca6e44a08d497630425e5ecd-wojtowiczem]
Subject: RE: NIH licensing

From: Myles, Renate (NIH/OD) [E]
Sent: Wednesday, July 31, 2019 4:03 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Cc: Fine, Amanda (NIH/OD) [E] <amanda.fine@nih.gov>; Wojtowicz, Emma (NIH/OD) [E] (emma.wojtowicz@nih.gov) <emma.wojtowicz@nih.gov>
Subject: FW: NIH licensing

Please review:

b5

From: Myles, Renate (NIH/OD) [E]
Sent: Wednesday, July 31, 2019 3:40 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>; Hallett, Adrienne (NIH/OD) [E] <adrienne.hallett@nih.gov>; Berkson, Laura (NIH/OD) [E] <laura.berkson@nih.gov>

Cc: Fine, Amanda (NIH/OD) [E] <amanda.fine@nih.gov>; Wojtowicz, Emma (NIH/OD) [E] <emma.wojtowicz@nih.gov>
Subject: RE: NIH licensing

Hi Mark:

The letter looks good to me.

b5

Thanks,
Renate

From: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Sent: Wednesday, July 31, 2019 2:55 PM
To: Hallett, Adrienne (NIH/OD) [E] <adrienne.hallett@nih.gov>; Myles, Renate (NIH/OD) [E] <mylesr@mail.nih.gov>; Berkson, Laura (NIH/OD) [E] <laura.berkson@nih.gov>
Cc: Fine, Amanda (NIH/OD) [E] <amanda.fine@nih.gov>; Wojtowicz, Emma (NIH/OD) [E] <emma.wojtowicz@nih.gov>
Subject: RE: NIH licensing

Unless you have comments, this should be final. Could you review it please before I send it out?

From: Hallett, Adrienne (NIH/OD) [E] <adrienne.hallett@nih.gov>
Sent: Wednesday, July 31, 2019 9:27 AM
To: Myles, Renate (NIH/OD) [E] <mylesr@mail.nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Berkson, Laura (NIH/OD) [E] <laura.berkson@nih.gov>
Cc: Fine, Amanda (NIH/OD) [E] <amanda.fine@nih.gov>; Wojtowicz, Emma (NIH/OD) [E] <emma.wojtowicz@nih.gov>
Subject: RE: NIH licensing

Okay by me.

From: Myles, Renate (NIH/OD) [E] <mylesr@mail.nih.gov>
Sent: Wednesday, July 31, 2019 9:00 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Hallett, Adrienne (NIH/OD) [E] <adrienne.hallett@nih.gov>; Berkson, Laura (NIH/OD) [E] <laura.berkson@nih.gov>
Cc: Fine, Amanda (NIH/OD) [E] <amanda.fine@nih.gov>; Wojtowicz, Emma (NIH/OD) [E] <emma.wojtowicz@nih.gov>
Subject: FW: NIH licensing

Hi Mark, Adrienne and Laura:

Can we respond to the reporter about the letter to FC since we've responded already on this topic? b5

b5

b5

From: Andrew Siddons <andrewsiddons@cqrollcall.com>
Sent: Wednesday, July 31, 2019 8:00 AM
To: Myles, Renate (NIH/OD) [E] <mylesr@mail.nih.gov>
Subject: NIH licensing

Hi Renate -- I hope all is well. As you are probably aware a few advocacy groups are calling attention to the NIH's licensing practices and asking for more transparency and more consideration of pricing when granting licenses... I'm referring specifically to the letter KEI sent last week (link below) and the letter that Patients for Affordable Drugs sent Tuesday (attached). Additionally, Senators Van Hollen and Scott are planning to introduce a bill related to drugs that benefit from NIH research, so I'm trying to write a story about this broader issue.

I know you can't comment on pending legislation but maybe you could comment more broadly with the NIH's position on licensing, prices and access. It woudl be great to get a response by early this afternoon. Thanks!

https://www.keionline.org/wp-content/uploads/KEI_Letter_HouseOversightCommittee_-NIH_Lack_of_Transparency_22July2019.pdf

Andrew Siddons
CQ Roll Call
Office: 202-650-6441
Mobile: b6

From: Lambert, Richard (NIH/NIAID) [C] [/O=NIH/OU=NIHEXCHANGE/CN=NIAID/CN=LAMBERTR]
Sent: 1/3/2017 5:29:38 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]; Mowatt, Michael (NIH/NIAID) [E] [/O=NIH/OU=NIHEXCHANGE/cn=NIAID/cn=MMOWATT]; Amar, Anna (NIH/NCI) [E] [/O=NIH/OU=Nihexchange/cn=niaid/cn=aamar]
Subject: FW: [Ip-health] NIH grant for "Development of an Intellectual Property (IP) Strategy for the Commercial Advancement of a Direct Phase II SBIR-Funded technology

Another FYI

Richard A. Lambert
Contractor
National Institute of Allergy and Infectious Diseases
National Institutes of Health
U.S. Department of Health and Human Services
5601 Fishers Lane, Rm. 2G47, MSC 9804
Bethesda, MD 20892-9804
(Courier: Rockville, MD. 20852)
301.496.2644 main officeline
240.627.3706 direct line
FAX 240.627.3117
lambertr@niaid.nih.gov

This message is intended for the exclusive use of the recipient(s) identified above. The information in this email and any of its attachments may be confidential and/or sensitive and should not be retained, disseminated, distributed or copied by or to persons not authorized to receive such information. If you receive this message in error please inform the sender and delete it immediately from your mailbox or any other storage devices. The National Institute of Allergy and Infectious Diseases (NIAID) shall not accept liability for any unauthorized statements made by the sender in this message.

-----Original Message-----
From: Michael H Davis [mailto:m.davis@csuohio.edu]
Sent: Tuesday, January 03, 2017 12:17 PM
To: Jamie Love <james.love@keionline.org>; Ip-health <ip-health@lists.keionline.org>
Subject: Re: [Ip-health] NIH grant for "Development of an Intellectual Property (IP) Strategy for the Commercial Advancement of a Direct Phase II SBIR-Funded technology

They won't march in because they don't know anything about prices but they know all about intellectual property? Is this agency out of its mind?

Sent from my T-Mobile 4G LTE Device

-------- Original message --------
From: Jamie Love <james.love@keionline.org>
Date: 1/3/17 12:03 PM (GMT-05:00)
To: Ip-health <ip-health@lists.keionline.org>
Subject: [Ip-health] NIH grant for "Development of an Intellectual Property (IP) Strategy for the Commercial Advancement of a Direct Phase II SBIR-Funded technology

https://projectreporter.nih.gov/project_info_description.cfm?aid=9253581&icde=32443948

Apparently the NIH will give you a grant to help you patent the heck out of a technology where they are also funding the research.

Project Number: 1SB1HL137591-01
Former Number: 2SB1HL131050-03
Contact PI / Project Leader: KARLSSON, SVEN M

Title: DEVELOPMENT OF AN INTELLECTUAL PROPERTY (IP) STRATEGY FOR THE COMMERCIAL ADVANCEMENT OF A DIRECT PHASE II SBIR-FUNDED HUMAN PLATELET BIOREACTOR Awardee Organization: PLATELET BIOGENESIS, INC.

PROJECT SUMMARY/ABSTRACT

Platelet BioGenesis is developing a microfluidic bioreactor to produce human platelets at clinical scale. Platelets are the 'band-aids' of the bloodstream, responsible for clot formation and blood vessel repair.

Low platelet count is a significant consequence of cancer treatment, transplant, and surgery, for which plate- lets are a critical first-line therapy to prevent mortality due to uncontrolled bleeding. Platelets are
de- rived exclusively from volunteer donors. Risk of bacterial growth during room temperature storage limits plate- let shelf life to 5 days, 2 of which are expended by bacterial screening, and 1 during transport to hospitals. As a result blood centers typically do not have more than a 1.5-day platelet inventory available for transfu- sion, making platelet unit inventory especially vulnerable to routine depletion[1, 2]. To address this ma- jor unmet need we are developing a platelet bioreactor that reproduces key features of adult bone marrow (physiological
microenvironment) to trigger platelet production from human induced pluripotent stem cells (hiP- SCs, a replenishable source of progenitor cells which can be stored frozen for years) at clinical/commercial scale.
This SBIR CRP Program proposal for Technical Assistance (SB1) outlines a comprehensive intellectual property strategy for Platelet BioGenesis to develop a proprietary, patent protected technology to produce cGMP-compliant human bioreactor-derived platelets at commercial scale for clinical use in 3 specific aims: Aim 1. Understanding the Patent Landscape.
We will work with IP counsel to: (1) identify and assess licens- ing various third party patents and patent applications related to megakaryocyte differentiation protocols and the platelet bioreactor, (2) perform further patent searches (landscape and/or freedom to operate) to ensure that we are able to commercialize our technology without infringement, and/or (3) identify any additional third party patents that may be licensed by us to further improve our competitive commercial position. Aim 2. Protecting Proprietary Technology to Enable Commercialization. We will work with IP counsel to identify intellectual property generated by us and will formulate a strategy for protecting such intellectual prop- erty, either by filing patent applications or ensuring that the technology is maintained as a trade secret. Aim 3. IP Agreements.
We will work with the IP counsel to: (1) review our non-disclosure agreements, em- ployment or consultant agreements to ensure the ownership and protection of our intellectual property, and (2) negotiate and enter into license agreements with cGMP-compliant hiPSC suppliers for access to relevant cell lines. cGMP-hiPSC line master banks will be maintained and differentiated into megakaryocytes under estab- lished supply agreements using proprietary cell culture protocols.

Public Health Relevance Statement:

PROJECT NARRATIVE Human platelets are presently derived exclusively from volunteer donors and have a shelf life of 5 days, mak- ing platelet unit inventory sensitive to depletion and putting platelet recipients at risk of sepsis and viruses dur- ing surgery, pregnancy and birth, cancer/HIV/burn-treatment, and transplant. There are currently no licensed therapeutics that immediately increase platelet counts, and insufficient platelet supply to meet projected US demand (~2.3M platelet units/year in 2013). Platelet BioGenesis has: identified cGMP-compliant hiPSC lines, validated megakaryocyte differentiation protocol and platelet storage-permissive media, and established a mi- crofluidic bioreactor to rapidly trigger functional platelet production at clinical/commercial scale. We now seek to develop a comprehensive IP strategy for linking these key technologies, which is necessary to advance bio- reactor-derived platelets (bdPLTs) for clinical use.

--
James Love. Knowledge Ecology International http://www.keionline.org/donate.html
KEI DC tel: +1.202.332.2670, US Mobile: +1.202.361.3040, Geneva Mobile: +41.76.413.6584, twitter.com/jamie_love

---

Ip-health mailing list
Ip-health@lists.keionline.org
http://lists.keionline.org/mailman/listinfo/ip-health_lists.keionline.org

---

Ip-health mailing list
Ip-health@lists.keionline.org
http://lists.keionline.org/mailman/listinfo/ip-health_lists.keionline.org

From: Plude, Denise (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/CN=RECIPIENTS/CN=PARKSDE]
Sent: 5/15/2017 4:38:45 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]
Subject: RE: NIH response to KEI on march-in

The letter was cleared by Drs. Collins and Tabak and is now at OS awaiting their clearance (it was assigned to NIH for Direct Reply with OS clearance). Once we receive OS clearance, we'll have Dr. Collins sign the final and send. If OS has any remarks/edits, Exec Sec will let us know.

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, May 15, 2017 11:24 AM
To: Plude, Denise (NIH/OD) [E] <pludede@mail.nih.gov>
Cc: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Subject: NIH response to KEI on march-in

Denise:

Do you have a way to check on that status of this pending response from FC? Is it under review by HHS?

THanks

Mark L. Rohrbaugh, Ph.D., J.D.
Special Advisor for Technology Transfer
Director, Division of Technology Transfer and Innovation Policy
Office of Science Policy
Office of the Director
National Institutes of Health

From: Carr, Sarah (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/CN=OD/CN=CARRS]
Sent: 12/30/2016 7:14:11 PM
To: Wolinetz, Carrie (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=Wolinetzcdc9a]; Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]
CC: Elzarrad, Mohammed (NIH/OD) [E] [/O=NIH/OU=Nihexchange/cn=recipients/cn=elzarradmk]
Subject: FW: WF 352363 - FYI
Attachments: Re: From Dr. Kathy Hudson -- In response to your correspondence to Secretary Burwell

This is just fyi.

From: Plude, Denise (NIH/OD) [E]
Sent: Friday, December 30, 2016 2:06 PM
To: Carr, Sarah (NIH/OD) [E] <CarrS@OD.NIH.GOV>
Subject: WF 352363 - FYI

Work Folder Information
Work Folder: WF 352363
Process: FYI
Program Analyst: Whitfield, Michelle D. (NIH/OD) [E]
Due Date:
WF Subject: Writes in response to the response he received from Dr. Hudson regarding NIH's decision to not use its royalty-free rights to expand access to enzalutamide, a treatment for prostate cancer (Xtandi).
IC: od_osp
From: Davis, Paul
To: Hudson, Kathy
Remarks: FYI for OER, OSP, OTT, OCPL, NCI, and OGC.

From: Paul Davis [pdavis@keionline.org]
Sent: 12/22/2016 9:25:11 PM
To: NIH Executive Secretariat [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=EXECSEC1]; Hudson, Kathy (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=Hudsonkl]
CC: James Packard Love [james.love@keionline.org]
Subject: Re: From Dr. Kathy Hudson -- In response to your correspondence to Secretary Burwell

22 December, 2016

Dear Dr. Hudson,

I am in receipt of your email regarding the decision by the NIH to reject the proposal that the NIH's royalty-free rights be exercised in order to expand access to enzalutamide, a treatment for prostate cancer. Enzalutamide is priced so aggressively worldwide that patients in developing countries have limited or no access.

Please share with Secretary Burwell that we note the fact that she opted out of an opportunity to take the side of poor cancer patients living in developing countries, in a case where the U.S. government holds rights in a federally funded invention, and a large Japanese drug company is charging excessive and unaffordable prices. Her decision to side with Astellas is consequential, for those cancer patients. She should reflect on this, as she leaves the federal government to a series of what are likely to be well-paid and prestigious positions in the non-profit and corporate world, attending future Davos conferences and the like.

As per your request, we will share your response with the other letter signatories. This will assure that they, also, will be reflecting on the Secretary's negative decision against patients, heading towards the future.

Sincerely,

Paul Davis, KEI

—

Paul Davis • pdavis@keionline.org
Knowledge Ecology Int'l
+1 202 817 0129
Skype/IM: pdavisx

> On Dec 20, 2016, at 3:20 PM, NIH Executive Secretariat <NIHExecSec@nih.gov> wrote:
>
> Dear Mr. Davis:
>
> This e-mail is to clarify the position of the National Institutes of Health (NIH) concerning the use of government authorities to address the issues you raised regarding Xtandi®. In a June 20, 2016 letter from Dr. Francis Collins, Director of the NIH, to Andrew Goldman, Knowledge Ecology International, the NIH declined to use the government's march-in authorities found at 35 U.S.C. §203 or to exercise the government's non-exclusive royalty-free government use license for Xtandi® (enzalutamide). The NIH has no additional information at this time that would compel it to reverse this decision

In addition, I was able to meet with your colleagues James Love, Andrew Goldman, and Zach Struver on November 7, 2016. Thank you again for coming to NIH and providing more information about your concern about barriers to drug access for patients in middle- and lower-income countries.

Please share this response with the organizations that signed the October 17, 2016, e-mail to Secretary Burwell.

Sincerely,

Kathy Hudson, Ph.D.
Deputy Director for Science, Outreach and Policy

From: Joe Allen [jallen@allen-assoc.com]
Sent: 12/20/2016 2:39:19 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]; Robert Hardy [rhardy@cogr.edu]; Hammersla, Ann (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=Recipients/cn=hammerslaa]
Subject: Re: Fwd: NYT: Harnessing the U.S. Taxpayer to Fight Cancer and Make Profits

you might pass this along to Ashley who was asking if Andrew Pollack was involved in last week's anti Bayh-Dole article. He wasn't but sure had his fingerprints on this one.

On 12/19/2016 8:57 PM, Rohrbaugh, Mark (NIH/OD) [E] wrote:

Sent from

Health

Harnessing the U.S. Taxpayer to Fight Cancer and Make Profits

By MATT RICHTEL and ANDREW POLLACK DEC. 19, 2016

Dr. Steven Rosenberg, left, who has led the surgery branch at the National Cancer Institute for 42 years, and Dr. Arie Belldegrun, the founder of Kite Pharma. Credit Jesse Dittmar (left) and Emily Berl (right) for The New York Times

Enthusiasm for cancer immunotherapy is soaring, and so is Arie Belldegrun's fortune.

Dr. Belldegrun, a physician, co-founded Kite Pharma, a company that could be the first to market next year with a highly anticipated new immunotherapy treatment. But even without a product, Dr. Belldegrun has struck gold.

His stock in Kite is worth about $170 million. Investors have profited along with him, as the company's share price has soared to about $50 from an initial price of $17 in 2014.

The results reflect widespread excitement over immunotherapy, which harnesses the body's immune system to attack cancer and has rescued some patients from near-certain death. But they also speak volumes about the value of Kite's main scientific partner: the United States government.

Kite's treatment, a form of immunotherapy called CAR-T, was initially developed by a team of researchers at the National Cancer Institute, led by a longtime friend and mentor of Dr. Belldegrun. Now Kite pays several million a year to the government to support continuing research dedicated to the company's efforts.

The relationship puts American taxpayers squarely in the middle of one of the hottest new drug markets. It also raises a question: Are taxpayers getting a good deal?

Defenders say that the partnership will likely bring a lifesaving treatment to patients, something the government cannot really do by itself, and that that is what matters most.

Critics say that taxpayers will end up paying twice for the same drug — once to support its development and a second time to buy it — while the company reaps the financial benefit.

"If this was not a government-funded cancer treatment — if it was for a new solar technology, for example — it would be scandalous to think that some private investors are reaping massive profits off a taxpayer-funded invention," said James Love, director of Knowledge Ecology International, an advocacy group concerned with access to medicines.

Photo

Dr. Rosenberg and Dr. Belldegrun in the mid-1980s. Dr. Belldegrun became a research fellow for Dr. Rosenberg at the cancer institute in 1985. Credit Kite Pharma

The debate goes squarely to one of the nation's most vexing challenges: rising health care and drug prices. Kite is one of a growing number of drug and biotech companies relying on federal laboratories. Analysts expect the company to charge at least $200,000 for the new treatment, which is intended as a one-time therapy for patients.

While the law allows the government to demand drug-price concessions from its private-sector partners, the government has declined to do so with Kite and generally disdains the practice.

Insisting on lower prices, federal researchers say, would drive away innovative partners that speed the drug-development process and benefit patients. But with the government doing so much pivotal research, others say that the private sector cannot afford to walk away.

"The market is so reliant on the knowledge and know-how that comes out of the government and academic labs," said Dr. Aaron Kesselheim, director of the Program on Regulation, Therapeutics and Law at Brigham & Women's Hospital in Boston.

Price curbs, he said, "would not suddenly lead to a total abandonment of this pipeline. It couldn't possibly."

Drug makers would be especially unlikely to turn away from immunotherapy, where the promising science has set off a "gold rush mentality," according to Mark Edwards of Bioscience Advisors, a company which tracks pharmaceutical licensing deals.

The National Institutes of Health, the parent agency of the National Cancer Institute, currently has about 400 cooperative research agreements with companies, and licenses hundreds of patented inventions for private-sector development.

Kite executives and national health officials characterize their partnership as a model arrangement in a system established by Congress three decades ago. The system has given birth to the cancer drug Taxol, the AIDS drug Prezista, two cervical cancer vaccines and a widely used test for H.I.V. infection, among other innovations.

Continue reading the main story

Photo

Dr. Rosenberg in his lab at the cancer institute in Bethesda, Md. Partnerships between government labs and drug companies are "absolutely essential or many discoveries will not see the light of day," he said. Credit Jesse Dittmar for The New York Times

Kite's first drug, called KTE-C19, could help thousands of patients each year in the United States with certain blood cancers. If it succeeds, it could generate sales of $1 billion to $2 billion annually, according to Wall Street analysts, making it among the most lucrative drugs to come from government research.

But the government's share of any Kite success would be modest, much lower than some academic research groups have wrangled in immunotherapy deals worth hundreds of millions of dollars. Federal officials counter that the reward to the taxpayer is not money but the drug itself.

"This is exactly the way things should work," said Dr. Steven Rosenberg, who has led the surgery branch at the National Cancer Institute for 42 years and led development of Kite's drug. Such partnerships, he said, are "absolutely essential or many discoveries will not see the light of day."

Moreover, government officials say, companies in such deals must take significant financial risks and expenditures on their own, without any guarantee that the drug will be approved.

Kite says it has spent more than $200 million on research and development, including running larger clinical trials than those conducted by the cancer institute, and recently spent about $30 million to build a factory that will be able to make treatments for up to 5,000 patients a year.

Setting the price of the drug, Dr. Rosenberg said, "is for the marketplace."

A Public-Private Partnership

Like many business deals, this one began with a personal relationship — in this case between Dr. Rosenberg and Dr. Belldegrun.

After finishing medical school in his native Israel, performing surgery in helicopters for the Israeli armed forces, and completing residency at Brigham & Women's Hospital, Dr. Belldegrun became a research fellow for Dr. Rosenberg at the N.C.I. It was 1985, and Dr. Belldegrun was put to work on a new project of Dr. Rosenberg's — extracting tumor-fighting immune cells from cancer patients, multiplying them in the laboratory, and putting them back in.

"He was one of the more outstanding fellows to come through," said Dr. Rosenberg, 76, who is widely considered a cancer research luminary.

Continue reading the main story

Photo

Dr. Belldegrun, center, at the Nasdaq stock exchange, where Kite Pharma is listed. The company was founded in 2009 and went public in 2014. Credit Nasdaq, 2016

When the fellowship ended in 1988, Dr. Belldegrun became a prominent surgeon at the University of California, Los Angeles, but the two men stayed in touch.

Eventually, Dr. Belldegrun, 67, got the entrepreneurial bug. He co-founded a biotech company, Agensys, which was acquired by a bigger company for more than $500 million. He was also involved with Cougar Biotechnology, which developed the prostate cancer drug Zytiga and was acquired by Johnson &

Johnson for $1 billion in May 2009. A month later, Dr. Belldegrun formed Kite with a group of colleagues and investors to pursue cancer immunotherapy.

That same month, a Florida marine contractor named Eric Karlson, whose non-Hodgkin's lymphoma was advancing despite four prior treatments, became the first patient treated by Dr. Rosenberg with what would eventually become KTE-C19. The treatment entailed removing some of Mr. Karlson's immune system T cells from his blood, genetically engineering them to recognize and fight his cancer, multiplying the T cells to huge numbers in the laboratory and transferring them back into his body. After two such treatments, Mr. Karlson remains alive and cancer-free eight years later.

Kite initially thought it would pursue an approach to immunotherapy known as cancer vaccines, but in 2010, Dr. Belldegrun visited Dr. Rosenberg and was shown the X-rays of Mr. Karlson and of a second patient.

Dr. Belldegrun was bowled over. "I had no doubt that this is going to be a drug and, more than that, it will become a platform for multiple products," he recalled. "We never looked back."

Over the next two years, the National Cancer Institute worked out a deal with Kite that was signed in 2012. It was the first of eight contracts between the government and the company that generally take two forms.

In one type of contract, Kite licenses patented inventions and agrees to pay the government royalties, roughly 5 percent of sales of any commercial product arising from a particular patent. However, there is no such license specifically for KTE-C19 because the underlying treatment was not patented by the N.C.I., so royalties will be minimal.

Officials say the agency did not apply for a patent because the treatment was similar to what others had been developing. Also, at the time the treatment was first created, in 2007, immunotherapy was considered to have dim commercial prospects.

"Back then, we didn't even think about commercial aspects," said Dr. James N. Kochenderfer, a scientist at the agency who designed the treatment when working in Dr. Rosenberg's group.

Under the second type of contract, known as a cooperative research and development agreement, Kite provides money to the N.C.I. to support research.

Kite is now paying $3 million a year to Dr. Rosenberg's lab and has provided $7.5 million to it in total since 2012. Based on its regulatory filings, Kite is paying $7.8 million a year for research agreements and licenses in total, with at least $4 million of that going to the cancer institute and the rest to academic or corporate partners.

The taxpayer has invested, too. Dr. Rosenberg estimated that the government has spent roughly $10 million over the years on what has become KTE-C19. He said Kite's $3 million a year is about equal to the taxpayer funding in that area and has helped speed research.

These days, researchers from Kite and the cancer institute, typically including Dr. Rosenberg and Dr. Belldegrun, confer by conference call every other Thursday for 90 minutes. Kite employees have spent long periods at the N.C.I., learning how to manufacture the therapy and how to treat patients in advance with chemotherapy.

"We shouldn't underestimate the value and the importance of N.I.H., not only to Kite but to the whole field of engineered T-cell therapy," Dr. Belldegrun said.

When Kite signed its first deal with the cancer agency, he said, it "tapped into six years of monumental work that they had done."

Some immunotherapy competitors marvel at the company's coup in tapping into the agency's expertise. "They got 20 years of research all together in one scoop," said Dr. Carlos Paya, chief executive of Immune Design, which is pursuing a different approach.

But government officials say few, if any, other companies were interested in the technology at the time Dr. Belldegrun came calling. Dr. Rosenberg said that before Kite, a few companies, including Johnson & Johnson, had looked at an earlier version of his technology but were wary because treatment involved processing each patient's cells.

Government-developed technology available to be licensed to companies is posted on the website of the National Institutes of Health. And when the agency intends to grant a license to a particular company, it publishes that in the Federal Register, inviting public comment and possible competing offers. Both steps were taken in the case of Kite, officials said.

Kite did not get everything the cancer institute has developed in the field. Some other companies, including Opus Bio and Bluebird Bio, got rights to some products, in part because the companies had special expertise that the agency's researchers desired. But Kite seems to have gotten the balance of them and N.C.I. technology accounts for the majority of its pipeline of possible products, though the company is diversifying.

Photo

A slide that Kite Pharma used in presentations to potential investors pointed out the company's relationship with Dr. Rosenberg.

Dr. Rosenberg professes no interest in the business side of the Kite relationship. He does not own stock in any company, even Kite, though he could get up to $150,000 a year in patent royalties if some of Kite's efforts pay off.

Dr. Belldegrun, in contrast to his mentor, has commercial flair. He is known for his sharp business suits, lives in the Bel-Air neighborhood of Los Angeles, and seems as comfortable on Wall Street or in high society as in the operating room.

Kite's relationship with the N.C.I. is an important part of its appeal to investors. In some presentations, Dr. Belldegrun has shown a photograph of himself with Dr. Rosenberg in their younger days. And he persuaded Dr. Rosenberg to speak at Kite's first big meeting for investors in June 2015, the only time he has ever spoken to Wall Street.

In emails obtained through a Freedom of Information Act request by Knowledge Ecology International, Dr. Belldegrun praised Dr. Rosenberg's talk and sent him copies of investment reports from the conference written by Wall Street analysts.

"Thank you for making the effort to come to NY," Dr. Belldegrun wrote. "I heard only raving reviews about your presence and presentation."

A 'Reasonable' Question

The reliance of private companies on government-funded research goes well beyond obvious cases like Kite. In many instances, companies work with universities or medical centers that, in turn, have been funded from the $32 billion annual budget of the National Institutes of Health.

Kite's two main competitors, Novartis and Juno Therapeutics, for instance, derived similar immunotherapy treatments largely from academic institutions, developed at least in part with government funding. Novartis has a relationship with the University of Pennsylvania, and Juno with the Memorial Sloan Kettering Cancer Center, the Fred Hutchinson Cancer Research Center and Seattle Children's Hospital.

"For the most important drugs you'll see some public-sector involvement," said Bhaven Sampat, an associate professor of health policy and management at Columbia University. He was one author of a study that found that 9 percent of all drugs approved between 1988 and 2005 were based directly on a patent held by the public sector. But 47.8 percent of the drugs relied at least indirectly on some federally funded research.

Continue reading the main story

Photo

The linked image cannot be displayed. The file may have been moved, renamed, or deleted. Verify that the link points to the correct file and location.

Eric Karlson at his home on Marco Island, Fla., this month. Mr. Karlson's non-Hodgkin's lymphoma was successfully treated by Dr. Rosenberg with what would eventually become KTE-C19. Credit Scott McIntyre for The New York Times

The figures were higher for more medically important drugs: 17.4 percent had a direct public-sector patent, while 64.5 percent had at least an indirect public-sector influence.

These figures are up sharply from before the 1980s. Such partnerships and licensing deals were encouraged by the 1980 Bayh-Dole and Stevenson-Wydler Acts, and the 1986 Federal Technology Transfer Act. The laws are credited with jump-starting the biotechnology industry.

But from the beginning, some people questioned whether taxpayers were getting a bad deal.

Perhaps the best-known drug developed from a cooperative research and development agreement — the cancer drug Taxol — was the subject of several congressional hearings in the early 1990s that investigated whether the drug's maker, Bristol-Myers Squibb, charged too much and whether the government recouped enough of its investment. In the end, the pricing was left unchanged.

The N.I.H. argues that if it imposes pricing restrictions, it won't get partners. In fact, in 1995, it struck from its negotiating tactics a goal that prices be "reasonable."

"Companies will not take technologies from us if we say the government will decide in the future what the price will be," said Mark Rohrbaugh, who ran the technology transfer office at the institutes from 2001 to 2013 and is now an adviser to the agency. After the "reasonable price" clause was struck, he said, there was a threefold increase in partnership deals.

The N.I.H. can collect royalties from successful products to help offset the costs of the research, but so far these royalties have been small, amounting to an estimated $135 million in the last fiscal year from 870 licenses, with the bulk of the money coming from a small number of drugs.

“We’re not preoccupied with financial value,” Dr. Rohrbaugh said. “Our mission is treatment of people and improving public health.”

In that regard, the government’s bet on a small company like Kite, which might have seemed risky, appears to be paying off so far. Dr. Belldegrun has largely delivered on promises to raise money, assemble an experienced staff, build the factory, conduct clinical trials and begin to apply for regulatory approval. Once considered the underdog to Novartis and Juno, Kite might be the first reach the market.

Photo

Scans of Mr. Karlson’s body before and after his treatment. In the cross-sections on the left, the arrows point to signs of lymphoma in areas such as his armpits, chest, spleen and pelvis. Credit National Cancer Institute

Academic centers and companies often drive harder bargains in licensing technology. In some cases, academic centers own a stake in a company they license technology to, allowing them to reap a financial windfall if the company does well. Both the Hutchinson cancer center and Sloan Kettering have owned stock in Juno and are entitled to substantial payments — up to $350 million and $150 million — if Juno’s stock reaches certain levels.

The N.I.H. does not take equity positions in companies to avoid an appearance of a conflict of interest. So to critics of the government deals, drug prices are crucial to understanding taxpayer value. After all, they ask, is a drug truly widely available — which is what the government says is its measure of success — if it costs too much for some people?

Rachel Sachs, an associate law professor at Washington University in St. Louis and expert in innovation policy, said the government had every right to seek price concessions. She noted that the government, through Medicare and Medicaid, was effectively buying its inventions back from itself. "The public is paying for the research and to the extent that many people, if not most, will pay through public insurance, we're paying again," she said.

Hillary Clinton, in her campaign for president, promised to set new rules for federal support of research so that Americans "get the value they deserve" for the money taxpayers spend in supporting research. It is not clear how President-elect Donald J. Trump will approach these issues; he has said he favors reducing health care costs, but Republicans, who control Congress, too, have opposed government involvement in price setting.

One mechanism to control pricing already exists. It is called march-in rights, and it lets the N.I.H. take back control of a patent on an invention made with federal funding if the drug is not being made available to the public on reasonable terms. The tool has gone unused.

Earlier this year, Knowledge Ecology International and another advocacy group, the Union for Affordable Cancer Treatment, petitioned the agency to exercise march-in rights on Xtandi, a prostate cancer drug that was developed by federally funded researchers at U.C.L.A. It said the price in the United States of about $129,000 a year, two to four times that in other developed countries, meant the drug was not reasonably available. The effort was supported by other public interest groups and some Democratic members of Congress.

U.C.L.A. made more than $500 million by selling its royalty rights to the drug. But the N.I.H. declined to exercise its march-in rights on Xtandi, arguing that it was not qualified to judge whether a drug's price is reasonable and that a high price does not mean a drug is not being made available to the public.

"N.I.H. has made it clear that its job is not to decide prices of drugs, period," Dr. Rohrbaugh said

Kite says it has not decided what to charge for KTE-C19, but Dr. Belldegrun hinted that Kite's therapy might be relatively expensive because ideally it would be a single treatment that would cure the patient, not a drug that would have to be taken continuously. He added that Kite would take steps to make sure that everyone who needed the drug could get it.

Meantime, the relationship between Kite and the National Cancer Institute is expanding to develop treatments for other cancers, including one technique Dr. Rosenberg thinks could be used to attack solid tumors like colon, breast and lung cancer.

"The potential for broad applicability is huge," he said.

That could mean many lives saved and maybe more billion-dollar drugs for Kite and its investors, with the American taxpayer right in the middle of the deal.

Like the Science Times page on Facebook. | Sign up for the Science Times newsletter.

--

Joseph P. Allen
President
Allen and Associates
60704 Rt. 26, South
Bethesda, OH 43719
(W) 740-484-1814
(c) b6
www.allen-assoc.com

From: Shmilovich, Michael (NIH/NHLBI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7DFE19BFD1D443CEB700B9F22D159A90-SHMILOVM]
Sent: 8/30/2018 8:14:00 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Berkley, Dale (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5ee461c29f5045a49f0adf82caaa2f31-berkleyd]
CC: Deutch, Alan (NIH/NHLBI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=244d755700584812af36b5e787285647-deutcha]
Subject: Re: Sinotau and MTTI licenses

Ok, also. b5

From: "Rohrbaugh, Mark (NIH/OD) [E]" <rohrbaum@od.nih.gov>
Date: Thursday, August 30, 2018 at 15:37:54
To: "Shmilovich, Michael (NIH/NHLBI) [E]" <michael.shmilovich@nih.gov>, "Berkley, Dale (NIH/OD) [E]" <berkleyd@od.nih.gov>
Cc: "Deutch, Alan (NIH/NHLBI) [E]" <deutcha@nhlbi.nih.gov>
Subject: RE: Sinotau and MTTI licenses

Ok, b5

b5

From: Shmilovich, Michael (NIH/NHLBI) [E]
Sent: Thursday, August 30, 2018 3:24 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>
Cc: Deutch, Alan (NIH/NHLBI) [E] <deutcha@nhlbi.nih.gov>
Subject: Re: Sinotau and MTTI licenses

Mark— thanks for your comments. I'll modify accordingly. b4,b5

b4,b5

From: "Rohrbaugh, Mark (NIH/OD) [E]" <rohrbaum@od.nih.gov>
Date: Thursday, August 30, 2018 at 15:13:37
To: "Shmilovich, Michael (NIH/NHLBI) [E]" <michael.shmilovich@nih.gov>, "Berkley, Dale (NIH/OD) [E]" <berkleyd@od.nih.gov>
Cc: "Deutch, Alan (NIH/NHLBI) [E]" <deutcha@nhlbi.nih.gov>
Subject: RE: Sinotau and MTTI licenses

Misha:

b5

b5

Thanks
Mark

From: Shmilovich, Michael (NIH/NHLBI) [E]
Sent: Tuesday, August 28, 2018 9:24 AM
To: Deutch, Alan (NIH/NHLBI) [E] <deutcha@nhlbi.nih.gov>; Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: FW: Sinotau and MTTI licenses

Dale, Mark and Alan -- ...same for MTTI... please review.

From: James Love <james.love@keionline.org>
Sent: Monday, August 27, 2018 16:57
To: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>
Cc: Luis Gil Abinader <luis.gil.abinader@keionline.org>; Claire Cassedy <claire.cassedy@keionline.org>; Manon Ress <MANON.RESS@cancerunion.org>
Subject: Sinotau and MTTI licenses

Michael Shmilovich, Esq.
Senior Licensing and Patent Manager
National Heart, Lung and Blood Institute
National Institutes of Health
31 Center Drive
Room 4A29, MSC2479
Bethesda, MD
Email: shmilovm@mail.nih.gov

Dear Michael Shmilovich

Attached are two comments filed jointly by KEI and UACT, regarding licenses noticed in the federal register.

1. Prospective Grant of Exclusive Patent License: Radiotherapy for Metastatic Castration-Resistant Prostate Cancer, 83 FR 35667 (www.federalregister.gov/d/2018-16066)

2. Prospective Grant of Exclusive Patent License: Radiotherapeutics Against Somatostatin-Receptor Expressing Neuroendocrine Tumors, 83 FR 35663 (https://www.federalregister.gov/d/2018-16065)

James Love

--
James Love. Knowledge Ecology International
http://www.keionline.org
twitter.com/jamie_love

From: Baker, Rebecca (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=BAKERRG]
Sent: 3/30/2016 7:39:56 PM
To: Marshall, Lisa (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=SchwartzL]; Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]; Jorgenson, Lyric (NIH/OD) [E] [/O=NIH/OU=Nihexchange/cn=recipients/cn=jorgensonla]
CC: Hammersla, Ann (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=Recipients/cn=hammerslaa]
Subject: RE: Question (putting together the monthly report to the Secretary)

Yes, thanks so much Mark!

Best,
Rebecca

From: Marshall, Lisa (NIH/OD) [E]
Sent: Wednesday, March 30, 2016 3:40 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>; Jorgenson, Lyric (NIH/OD) [E] <jorgensonla@od.nih.gov>
Cc: Baker, Rebecca (NIH/OD) [E] <bakerrg@od.nih.gov>; Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Subject: RE: Question (putting together the monthly report to the Secretary)

Many thanks! Very helpful. Lisa

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Wednesday, March 30, 2016 3:39 PM
To: Marshall, Lisa (NIH/OD) [E]; Jorgenson, Lyric (NIH/OD) [E]
Cc: Baker, Rebecca (NIH/OD) [E]; Hammersla, Ann (NIH/OD) [E]
Subject: RE: Question (putting together the monthly report to the Secretary)

b5

From: Marshall, Lisa (NIH/OD) [E]
Sent: Wednesday, March 30, 2016 2:12 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>; Jorgenson, Lyric (NIH/OD) [E] <jorgensonla@od.nih.gov>
Cc: Baker, Rebecca (NIH/OD) [E] <bakerrg@od.nih.gov>
Subject: Question (putting together the monthly report to the Secretary)
Importance: High

Hi –

I'm putting together the Monthly Report for the HHS Secretary (a draft is attached). Rebecca Baker had the very good idea to b5 b5 Of course, I need this info ASAP so I can get this report to Drs. Hudson, Tabak, and Collins today. b5 Many thanks for your help! Lisa

---

From: Baker, Rebecca (NIH/OD) [E]
Sent: Wednesday, March 30, 2016 2:06 PM
To: Marshall, Lisa (NIH/OD) [E]
Cc: Schwetz, Tara (NIH/OD) [E]
Subject: RE: For your Review: Secretary's Monthly Report for April

I am not completely up to date.
Could you please ask Lyric Jorgenson and Mark Rohrbaugh?
Please feel free to copy me and say it was my idea.

Thanks,
Rebecca

From: Marshall, Lisa (NIH/OD) [E]
Sent: Wednesday, March 30, 2016 2:05 PM
To: Baker, Rebecca (NIH/OD) [E] <bakerrg@od.nih.gov>
Cc: Schwetz, Tara (NIH/OD) [E] <schwetzta@od.nih.gov>
Subject: RE: For your Review: Secretary's Monthly Report for April
Importance: High

Actually, Rebecca, the more I think about it, the more I think it would probably be a good idea to b5 b5 Dr. Collins can choose to remove if he wants (but I doubt it). Can I get a quick write-up from you on it (or would it be better to get it from someone else?)? b5 b5 Thanks so much, Lisa

---

From: Baker, Rebecca (NIH/OD) [E]
Sent: Wednesday, March 30, 2016 1:56 PM
To: Schwetz, Tara (NIH/OD) [E]; Marshall, Lisa (NIH/OD) [E]
Subject: RE: For your Review: Secretary's Monthly Report for April

Hi Lisa,

This report has gotten so much better, it's amazing.
Thank you for sending a clear message to the submitting offices.
I have no additional edits to this report.

b5

Thanks for your thoughts,

Rebecca

From: Schwetz, Tara (NIH/OD) [E]
Sent: Wednesday, March 30, 2016 12:02 PM

To: Marshall, Lisa (NIH/OD) [E] <MarshallL@od.nih.gov>; Baker, Rebecca (NIH/OD) [E] <bakerrg@od.nih.gov>
Subject: RE: For your Review: Secretary's Monthly Report for April

Please find attached my edits/comments. Should you have any questions, do let me know.

Best,

Tara A. Schwetz, PhD
Immediate Office of the Director
National Institutes of Health
Building 1, Suite 108
Bethesda MD, 20892
Office: 301-451-5064 | Cell: b6
tara.schwetz@nih.gov

From: Marshall, Lisa (NIH/OD) [E]
Sent: Wednesday, March 30, 2016 11:31 AM
To: Baker, Rebecca (NIH/OD) [E] <bakerrg@od.nih.gov>
Cc: Schwetz, Tara (NIH/OD) [E] <schwetzta@od.nih.gov>
Subject: For your Review: Secretary's Monthly Report for April
Importance: High

Hi Rebecca,
Looks like Tara is out so hopefully you can clear/edit today. It seems our note about shortening submissions "took," because the report is only 3 pages long this month (yay!). Once I get your okay, I will package for Drs. Hudson's, Tabak's, Collins review. Many thanks, Lisa

---

From: Hammersla, Ann (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/CN=RECIPIENTS/CN=HAMMERSLAA]
Sent: 3/30/2016 7:36:00 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]
Subject: RE: March 28 Congressional re: Xtandi

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Wednesday, March 30, 2016 3:30 PM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Subject: FW: March 28 Congressional re: Xtandi

b5

From: Jorgenson, Lyric (NIH/OD) [E]
Sent: Wednesday, March 30, 2016 3:18 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Cc: Carr, Sarah (NIH/OD) [E] <CarrS@OD.NIH.GOV>
Subject: RE: March 28 Congressional re: Xtandi

Mark – thanks for starting this. b5

b5

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Wednesday, March 30, 2016 3:05 PM
To: Jorgenson, Lyric (NIH/OD) [E] <jorgensonla@od.nih.gov>
Cc: Carr, Sarah (NIH/OD) [E] <CarrS@OD.NIH.GOV>
Subject: RE: March 28 Congressional re: Xtandi

Lisa Marshall wanted a short write up for HHS on this matter. Thoughts on this draft?

b5

From: Jorgenson, Lyric (NIH/OD) [E]
Sent: Wednesday, March 30, 2016 2:42 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Cc: Carr, Sarah (NIH/OD) [E] <CarrS@OD.NIH.GOV>
Subject: RE: March 28 Congressional re: Xtandi

Well at least you got oodles of time!!!!!!!!!!!!!!!!! ☹

Is there anything I can do to help?

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Wednesday, March 30, 2016 2:42 PM
To: Jorgenson, Lyric (NIH/OD) [E] <jorgensonla@od.nih.gov>
Cc: Carr, Sarah (NIH/OD) [E] <CarrS@OD.NIH.GOV>
Subject: RE: March 28 Congressional re: Xtandi

Yes, I was told it was assigned to me to draft by Friday.

From: Jorgenson, Lyric (NIH/OD) [E]
Sent: Wednesday, March 30, 2016 2:16 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Cc: Carr, Sarah (NIH/OD) [E] <CarrS@OD.NIH.GOV>
Subject: FW: March 28 Congressional re: Xtandi

Heads up – have you seen this yet?

From: Allen-Gifford, Patrice (NIH/OD) [E]
Sent: Tuesday, March 29, 2016 5:22 PM
To: Wolinetz, Carrie (NIH/OD) [E] <carrie.wolinetz@nih.gov>; Jorgenson, Lyric (NIH/OD) [E] <jorgensonla@od.nih.gov>
Cc: Koeneman, Sandy (NIH/OD) [E] <Sandra.Koeneman@nih.gov>
Subject: March 28 Congressional re: Xtandi

Hi Carrie and Lyric –

We wanted to give you a heads up on the attached letter from Sen. Sanders, Rep. Doggett and 10 other Members of Congress recommending NIH hold public hearings regarding march-in rights. In accordance with how we assigned the letter from Rep. Doggett earlier this month, ES is asking OSP to take the lead in drafting the response, working with OER and OTT. OS has asked NIH for a draft response for SMB's signature, so ES will clear with other offices, as well as Drs. Hudson, Tabak and Collins.

Please let us know if you need anything in connection with this assignment.

Best,
Patrice

From:	Shmilovich, Michael (NIH/NHLBI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7DFE19BFD1D443CEB700B9F22D159A90-SHMILOVM]
Sent:	8/31/2018 1:47:59 AM
To:	Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Deutch, Alan (NIH/NHLBI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=244d755700584812af36b5e787285647-deutcha]; Berkley, Dale (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5ee461c29f5045a49f0adf82caaa2f31-berkleyd]
Subject:	Emailing: NIH to KEI re Sinotau 30Aug2018 v2.docx, NIH to KEI re MTTI 30Aug2018 v2.docx
Attachments:	NIH to KEI re Sinotau 30Aug2018 v2.docx; NIH to KEI re MTTI 30Aug2018 v2.docx

....Take 2.....

Please comment.

Your message is ready to be sent with the following file or link attachments:

NIH to KEI re Sinotau 30Aug2018 v2.docx
NIH to KEI re MTTI 30Aug2018 v2.docx

Note: To protect against computer viruses, e-mail programs may prevent sending or receiving certain types of file attachments. Check your e-mail security settings to determine how attachments are handled.

b5

b5

b5

b5

From: Vepa, Sury (NIH/NCATS) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=25B6C29F123544738FCBAD51627B2D23-VEPAS]
Sent: 7/19/2018 4:20:24 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Portilla, Lili (NIH/NCATS) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=9b03f548be224eb9b7b6167a32e9cc4a-portilll]
Subject: RE: Prospective Grant of Exclusive Patent License: Mutant IDH1 Inhibitors Useful for Treating Cancer to Apexx Oncology. Notice for comment published in 83 FR 29562.

Thanks, Mark. I incorporated your suggestions. Can I send these to Kei or do I need to clear these with OGC also.

Regards,

Sury

Phone: 301-827-7181
Cell: b6
E-Mail: sury.vepa@nih.gov

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Thursday, July 19, 2018 11:28 AM
To: Vepa, Sury (NIH/NCATS) [E] <sury.vepa@nih.gov>; Portilla, Lili (NIH/NCATS) [E] <portilll@mail.nih.gov>
Subject: RE: Prospective Grant of Exclusive Patent License: Mutant IDH1 Inhibitors Useful for Treating Cancer to Apexx Oncology. Notice for comment published in 83 FR 29562.

Nice job. Couple comments:

b5

From: Vepa, Sury (NIH/NCATS) [E]
Sent: Thursday, July 19, 2018 10:59 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Portilla, Lili (NIH/NCATS) [E] <portilll@mail.nih.gov>
Subject: FW: Prospective Grant of Exclusive Patent License: Mutant IDH1 Inhibitors Useful for Treating Cancer to Apexx Oncology. Notice for comment published in 83 FR 29562.

Hi Mark and Lili,

Please see below a draft response email to KEI. My responses are based on responses previously provided by NCI and NIAID. Would appreciate your suggestions before I send them to KEI.

Thanks,

Sury

b5

Sury

Phone: 301-827-7181
Cell: b6
E-Mail: sury.vepa@nih.gov

From: James Love [mailto:james.love@keionline.org]
Sent: Tuesday, July 10, 2018 4:35 PM
To: Vepa, Sury (NIH/NCATS) [E] <sury.vepa@nih.gov>
Cc: Luis Gil Abinader <luis.gil.abinader@keionline.org>; Claire Cassedy <claire.cassedy@keionline.org>; Manon Ress <manon.ress@keionline.org>; Thiru Balasubramaniam <thiru@keionline.org>
Subject: Re: Prospective Grant of Exclusive Patent License: Mutant IDH1 Inhibitors Useful for Treating Cancer to Apexx Oncology. Notice for comment published in 83 FR 29562.

July 10, 2018

Sury Vepa, Ph.D., J.D.,
Senior Licensing and Patenting Manager,
National Center for Advancing Translational Sciences
National Institutes of Health
Email sury.vepa@nih.gov

Re: Prospective Grant of Exclusive Patent License: Mutant IDH1 Inhibitors Useful for Treating Cancer to Apexx Oncology. Notice for comment published in 83 FR 29562.

https://www.federalregister.gov/documents/2018/06/25/2018-13486/prospective-grant-of-exclusive-patent-license-mutant-idh1-inhibitors-useful-for-treating-cancer

Dear Dr. Vepa,

Knowledge Ecology International (KEI) offers the following comments on the, “Prospective Grant of Exclusive Patent License: Mutant IDH1 Inhibitors Useful for Treating Cancer,” to Apexx Oncology, which was noticed in the Federal Register (83 FR 29562).

As far as the public can determine, Apexx Oncology is a secretive startup company. The only information we could find using a Google search about the company was a contest for a logo of the company. There is no record of a registered trademark for Apexx Oncology with the USPTO. No web page has been located. It is not obvious if Apexx Oncology is a new name for GeneXion Oncology (as indicated today), or a new company entirely, and in any case, there is next to nothing generally known about the company under either name.

When the NIH proposes giving an exclusive license on a patent to a company for which almost nothing is known, it should provide at the very least some basic information about the company. In seeking to respond to the first FR notice in this case, we had asked if GeneXion was owned by a company in Switzerland, but the NIH declined to answer. We don’t know who is on the board of directors, who the key staff are or if another company owns this company. We would like to know if any current or former NIH employees or contractors are part of the company.

We also seek to learn -- why this company was selected in the first place? Do they have people who have worked on this particular technology, or have some special expertise? And since the patents are fairly new, did the NIH have no reasonable prospects for a license to an entity with more resources and a stronger track record than a company that seems to barely exist?

Here are some general provisions that we recommend for an exclusive license by the NIH.

1. **No discrimination against US residents in pricing.**

Prices in the U.S. for any drug, vaccine, medical device or other health technology using the invention should not be higher than the median price charged in the seven countries with the largest gross domestic product (GDP), that also have a per capita income of at least 50 percent of the United States, as measured by the World Bank Atlas Method.

2. **Developing countries.**

The license should not be exclusive for countries with a per capita income that is less than 30 percent of the US.

3. **Transparency.**

The licensee should be required to file an annual report to the NIH, available to the public, on the research and development (R&D) costs associated with the development of any product that uses the invention, including reporting separately and individually the outlays on each clinical trial. We will note that this is not a request to see a company business plan or license application. We are asking that going forward the company be required to report on actual R&D outlays to develop the subject inventions.

4. **Reduce term of exclusivity when revenues are large.**

The exclusivity of the license in the U.S. should be reduced by one year for every $500 million in revenue equivalents, earned after the first $1 billion, where revenue equivalent is defined as global cumulative sales plus market entry rewards as well as government grants or tax credits, for the product or products using the invention.

Sincerely,

James Love
Knowledge Ecology International
james.love@keionline.org
https://keionline.org

--
James Love. Knowledge Ecology International
http://www.keionline.org/donate.html
KEI DC tel: +1.202.332.2670, US Mobile: +1.202.361.3040, Geneva Mobile: +41.76.413.6584,
twitter.com/jamie_love

From: Berkson, Laura (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=DAMIANOLD]
Sent: 4/6/2016 7:03:58 PM
To: Hudson, Kathy (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=Hudsonkl]; Baker, Rebecca (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=Bakerrg]; Hallett, Adrienne (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=Hallettaa07c]; Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]; Hammersla, Ann (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=Recipients/cn=hammerslaa]; Culhane, Ned (NIH/OD) [E] [/O=NIH/OU=Nihexchange/cn=recipients/cn=culhanee]; Jorgenson, Lyric (NIH/OD) [E] [/O=NIH/OU=Nihexchange/cn=recipients/cn=jorgensonla]
Subject: March-In article after House Approps hearing

Hi Kathy,

As promised, here is the Bloomberg article that got a lot of attention after FC's House Approps hearing regarding march-in/drug pricing. I've also included an article Mark shared that is written by Joe Allen, a former Bayh staffer, arguing against the use of march-In for drug control.

Let us know if you need anything else.

Laura

Laura Berkson, J.D.
Office of Legislative Policy & Analysis
National Institutes of Health
(301) 496-3471 | laura.berkson@nih.gov

NIH Open to Exercising Rights to Reduce High Drug Prices

March 16, 2016 12:06PM ET | Bloomberg First Word

(Bloomberg) -- National Institutes of Health would be willing to exercise the right it has to cut high prices charged for drugs developed with taxpayer dollars, agency Director Francis S. Collins says, Bloomberg BNA's Jeannie Baumann reports.

- "We are certainly open to considering it on a case-by-case basis," Collins tells House Appropriations Cmte panel
-
- HHS hasn't intervened on prices to date
-
- Rosa DeLauro, top Democrat on the Labor-HHS House Appropriations panel, says U.S. taxpayers are being "gouged" by high drug prices
-
- Americans are paying for drug development by funding the NIH and still pay higher price for drug at pharmacy, DeLauro says

NIH Pressured to Misuse Bayh-Dole to Control Drug Prices

By Joseph Allen, March 30, 2016

Anyone who imagines that running a federal agency would be fun should consider the plight of HHS Secretary Sylvia Burwell and NIH Director Francis Collins. How would you like to have prominent Members of Congress, "public interest" groups, and the media claiming that you have the power to lower drug costs to help desperately needy people, but you refuse to use it?

Secretary Burwell and Director Collins are facing formidable pressure to reinterpret the Bayh-Dole Act for the compulsory licensing of costly drugs arising from federally supported research. They may get some comfort knowing such actions aren't sanctioned by the law, or that caving in would devastate the U.S. drug development system. The stakes in their decision whether or not to "march-in" to control the price of Xtandi, a prostate cancer drug, are enormous.

And the pressure just increased another notch. On March 28, Senators Bernie Sanders,Elizabeth Warren, Al Franken, Patrick Leahy, Sheldon Whitehouse and Amy Klobuchar joined the leaders of the House Democratic Task Force on Prescription Drug Pricing urging Burwell and Collins to hold a meeting "to allow the public to engage in a dialogue with the Department of Health and Human Services and NIH in order to better understand its position on the use of march-in rights to address excessive prices."

If NIH joins in pursuing the swamp gas illusion that Bayh-Dole was intended to regulate drug pricing, we'll quickly learn that it's a lot easier getting into this morass than getting back out.

One of the greatest successes of the law is the development of life saving therapies from federally funded research. While no new drugs were developed under preceding policies, at least 200 new drugs and vaccines are now protecting human health through Bayh-Dole. The law gave companies confidence that universities and federal laboratories could be reliable research partners.

When passing Bayh-Dole, Congress was concerned that dominant businesses might license breakthrough inventions from universities to suppress them if they competed with lucrative products, so a "march-in" provision was adopted. If it's determined that good faith efforts are not being made to develop a university invention, the funding agency can insist that additional licenses are issued "upon terms that are reasonable under the circumstances…" March-ins can also be used if health or other emergencies arise and the licensee is unable to manufacture enough products to meet public needs. After 35 years the march-in provision has never needed to be invoked.

Decades after Bayh-Dole passed, two professors theorized that Congress intended the march-in provision to be used when drugs based on academic inventions are not reasonably priced (see *Hunting Bayh-Dole Vampires*). Recognizing the danger, Senators Bayh and Dole immediately replied that price controls are not sanctioned by their law. They knew what would happen under the professor's theory. Who would commercialize a university invention if the government could march in based on retroactive standards determining whether it's "reasonably priced?" And this would apply to any Bayh-Dole invention, not just drugs. Every agency would be free to make up their own criteria, which could change anytime at the whim of the bureaucracy. Companies would flee from academic partnerships– with good reason.

Senator Bayh added that if Congress ever wants such a provision, it must amend the statute and should define what it means by a "reasonable price." Nevertheless, several petitions have been filed with NIH over the years seeking to use march-ins to control drug prices– all of which were denied.

The latest attempt began on January 11, 2016 when fifty Members of Congress led by Rep. Lloyd Doggett (D-TX) wrote Secretary Burwell and Director Collins urging them to issue guidelines for marching in to control drug prices deemed unreasonably high. They suggested that one trigger could be when a drug made from a federally funded invention costs more in the U.S. than abroad. Disregarding Senator Bayh's admonition, the letter claims that agencies have such authorities under Bayh-Dole.

Demonstrating a careful coordination with the Congressional letter, two days later Knowledge Ecology International and the Union for Affordable Cancer Treatment filed a march-in petition against Xtandi, a prostate cancer drug based on a University of California patent made with NIH and Dept. of Defense funding. The petition alleges that Xtandi "is 2 to 4 times higher in the U.S. than in other high income countries, and that the 'march-in' provisions in the Bayh-Dole Act should be used to protect U.S. consumers from excessive prices." They add that since African American men have a higher incidence of prostate cancer than other groups, NIH and DoD "should be concerned that the high price of Xtandi may be contributing to systemic racial discrimination in medical care in the United States."

The petition asks NIH to grant an open license for any generic drug manufacturer to produce Xtandi. Publications ranging from *The Washington Post* to *Russia Today* covered the story.

On March 2, 2016, Secretary Burwell replied stating:

The NIH considered using its march-in authority to address drug pricing concerns in 2013 for Norvir (ritonavir) and Xalantan (lantanoprost), and in 2013 for the pricing of Norvir a second time… In each review, the NIH considered whether the marketed drug met the statutory requirements to justify the use of the march-in authority and determined that it did not.

NIH considers the application of the march-in statute on a case-by-case basis, and is prepared to use its authority if presented with a case where the statutory criteria are met regarding the commercialization and use of an NIH-funded, patented invention, and where march-in could in fact alleviate health or safety needs or address a situation where effective steps are not being taken to achieve practical application of the inventions. After consulting with the NIH, we believe the statutory criteria are sufficiently clear and additional guidance is not needed.

Immediately after hearing from Secretary Burwell, Rep. Doggett joined the calls for NIH to march-in on Xtandi. He was soon joined by eleven groups including Public Citizen, the American Medical Students Association, Universities Allied for Essential Medicines and the Alliance for Retired Americans .

It appeared as though this pressure was taking a toll when "*NIH Open to Exercising Drug Pricing Rights, Director Says*" appeared in *Bloomberg's Patent, Trademark & Copyright Journal's Afternoon Briefing* on March 16. Reporting on Dr. Collin's reply to the House Appropriations Subcommittee where he was pressed to march-in to control drug costs, the story claimed: "*The NIH would be open to exercising its 'march-in rights' to reduce high prices charged for drugs developed with taxpayer dollars, NIH Director Francis S. Collins said today*."

That set off alarms that either Sec. Burwell and Dr. Collins were not on the same page or that NIH was changing its position. However, Collin's answer was not accurately captured in the story:

We have looked at that situation several times in the past but have not felt that we have reached reasonable terms. But we are totally open to considering that on a case by case basis. We'll be glad to do that with other products that are brought forward for our consideration. We get it, that this is a serious issue.

Thus, Secretary Burwell and Dr. Collins are saying that each petition must be reviewed against the accepted march-in standards of Bayh-Dole. However, prominent Democratic Members of Congress working with a few interest groups are urging them to adopt an entirely new interpretation of the law. The ruling on the Xtandi petition will show which view prevails.

Reflecting on the dilemma, Thomas Peter Stossel and Joel M. Zinberg with the *American Enterprise Institute* noted in When fools march in:

National Institutes of Health officials just wisely rejected a petition, supported by 51 congressmen, to exercise "march-in" rights to discourage drug "price-gouging." The proposal didn't merely violate the explicit intent of a decades-old statute — the Bayh-Dole Act — it also revealed the legislators' ignorance of drug development and would have devastated medical innovation, while doing nothing to bring down drug costs.

NIH officials must continue to reject similarly misguided and politicized petitions. The future of American medicine depends on it.

Even if march-in powers could lower prices for this fraction of drugs, this congressional intervention risks chilling all drug development regardless of whether government funding played a direct role. Encouraging the government to seize patent rights in a non-emergency situation is a great way to discourage firms from developing and producing any new drugs.

Congress' failed political ploy asking NIH to employ march-in rights to control drug prices disregarded the spirit of the law, the best judgment of NIH officials and the interests of patients. Thankfully, Health and Human Services Secretary Sylvia Mathews Burwell understood the purpose of the law. Let's hope future petitions meet the same fate.

So let's keep our fingers crossed as we await the decision on Xtandi. If Secretary Burwell and Director Collins refuse to join this misguided quest to control drug prices, they are more likely to hears howls of protest than thanks from those who will benefit from preserving the world's leading drug development system. Perhaps that's a good definition of public service– doing the right thing knowing that your are more likely to be attacked than praised.

From: Amar, Anna (NIH/NCI) [E] [/O=NIH/OU=EXTERNAL (FYDIBOHF25SPDLT)/CN=RECIPIENTS/CN=7EC071C2DE2D4851A877079F59475AAE]

Sent: 4/20/2017 1:41:49 PM

To: Ano, Susan (NIH/NINDS) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ANOS]; Bailey, Brian (NIH/NHLBI) [E] [/O=NIH/OU=NIHEXCHANGE/cn=NCI/cn=BBAILEY]; Balakrishnan, Krishna (NIH/NCATS) [E] [/O=NIH/OU=EXTernal (FYDIBOHF25SPDLT)/cn=Recipients/cn=47d51e7d288c48529bccee3456c25c5e]; Bradley, David (NIH/NIDCR) [E] [/O=NIH/OU=NIHEXCHANGE/cn=nidcr/cn=bradleyda]; Carroll, Kathleen (NIH/NCI) [E] [/O=NIH/OU=EXTernal (FYDIBOHF25SPDLT)/cn=Recipients/cn=995d6aebf0814f44accf725bce001609]; Clarkson, Adam (NIH/OD/ORS) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ORS/cn=clarksona]; Cole, Eric (NIH/CC/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=Colee]; Collins, Dexter (NIH/FIC) [E] [/O=NIH/OU=EXTernal (FYDIBOHF25SPDLT)/cn=Recipients/cn=4ab454aeaa564667a63946a214c91161]; Conley, Vio (NIH/NCI) [E] [/O=NIH/OU=EXTernal (FYDIBOHF25SPDLT)/cn=Recipients/cn=4232ad9d95734271b1c6572a9ae24af5]; Davis, Belinda (NIH/NCCIH) [E] [/O=NIH/OU=NIHEXCHANGE/cn=NEI/cn=DAVISB]; Deutch, Alan (NIH/NHLBI) [E] [/O=NIH/OU=NIHEXCHANGE/cn=NHLBIOS/cn=DeutchA]; Driscoll, Claire (NIH/NHGRI) [E] [/O=NIH/OU=NIHEXCHANGE/cn=NHGRI/cn=cdriscol]; Eden, Henry (NIH/NIBIB) [E] [/O=NIH/OU=EXTernal (FYDIBOHF25SPDLT)/cn=Recipients/cn=80c6a1d015d84acbb02d6050862e5c44]; Fischer, Karen (NIH/NIDCD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=NIDCD/cn=FischerK]; Frisbie, Suzanne (NIH/NIAID) [E] [/O=NIH/OU=Nihexchange/cn=nci/cn=frisbies]; Guyton, Nicole (NIH/NCI) [E] [/O=NIH/OU=EXTernal (FYDIBOHF25SPDLT)/cn=Recipients/cn=386e9504fb61453dae662a191c74f925]; Hubbs, Alan (NIH/NCI) [E] [/O=NIH/OU=EXTernal (FYDIBOHF25SPDLT)/cn=Recipients/cn=363d84ddeec24266b22defe747ce0604]; Kim, Hyung-Suk (NIH/NINR) [E] [/O=NIH/OU=EXTernal (FYDIBOHF25SPDLT)/cn=Recipients/cn=4f1d9276be00404baad0a0cd57847e35]; Klun, Aida (NIH/NIDA) [E] [/O=NIH/OU=EXTernal (FYDIBOHF25SPDLT)/cn=Recipients/cn=44062a5f5b074dbc9e1fdb516b9fb03b]; Koelble, Peg (NIH/NHLBI) [E] [/O=NIH/OU=NIHEXCHANGE/cn=NHLBIOS/cn=KoelbleP]; Lauderdale, Kevin (NIH/NIGMS) [E] [/O=NIH/OU=NIHEXCHANGE/cn=NIGMS/cn=LauderdK]; Leff, Michelle (NIH/NIDA/IRP) [E] [/O=NIH/OU=EXTernal (FYDIBOHF25SPDLT)/cn=Recipients/cn=f786979339074839 8256f4f2dc947d0a]; Maurey, Karen (NIH/NCI) [E] [/O=NIH/OU=EXTernal (FYDIBOHF25SPDLT)/cn=Recipients/cn=918c32b0a9174941a3d2807a3ec25c2d]; Mcguinness, Charlotte (NIH/NCI) [E] [/O=NIH/OU=EXTernal (FYDIBOHF25SPDLT)/cn=Recipients/cn=3e8b8c2f398d49b5be30d91b9555c4e5]; Merchak, Todd (NIH/NIBIB) [E] [/O=NIH/OU=EXTernal (FYDIBOHF25SPDLT)/cn=Recipients/cn=c9e6d28184314159afd657cb8a2e11dc]; Mowatt, Michael (NIH/NIAID) [E] [/O=NIH/OU=NIHEXCHANGE/cn=NIAID/cn=MMOWATT]; Niebylski, Charles (NIH/NIDDK) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=Niebylskicd]; O'Donnell, Michael (NIH/NIA/IRP) [E] [/O=NIH/OU=EXTernal (FYDIBOHF25SPDLT)/cn=Recipients/cn=9f62fb96f41b4476b977756837ec2966]; Pillsbury, Patricia (NIH/NIGMS) [E] [/O=NIH/OU=NIHEXCHANGE/cn=NIGMS/cn=pillsbup1]; Portilla, Lili (NIH/NCATS) [E] [/O=NIH/OU=EXTernal (FYDIBOHF25SPDLT)/cn=Recipients/cn=1d3dbcee212e4583a0262200948735b6]; Rodriguez, Richard (NIH/NCI) [E] [/O=NIH/OU=EXTernal (FYDIBOHF25SPDLT)/cn=Recipients/cn=5c43750192ca4e0e890422519477dd41]; Rose, Ken (NIH/NCI) [E] [/O=NIH/OU=EXTernal (FYDIBOHF25SPDLT)/cn=Recipients/cn=fe6b99ce6b124b87a3623e353ed17e97]; Ryan, Megan (NIH/NIAAA) [E] [/O=NIH/OU=EXTernal (FYDIBOHF25SPDLT)/cn=Recipients/cn=4e2affc5240c48b5b46e46b1addbcfa2]; Salahuddin, Charles (NIH/NIMH) [E] [/O=NIH/OU=Nihexchange/cn=recipients/cn=salahuddinc]; Schneeweis, David (NIH/NEI) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=Schneeweisdmc33]; Silverman, Peter (NIH/NIAAA) [C] [/O=NIH/OU=EXTernal (FYDIBOHF25SPDLT)/cn=Recipients/cn=92d3a5a363c74b4a8fae1aa44ca0f787]; Solowiej, Anna (NIH/NHGRI) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=Solowieja]; Stackhouse, Thomas (NIH/NCI) [E] [/O=NIH/OU=EXTernal (FYDIBOHF25SPDLT)/cn=Recipients/cn=c2c44da4dc054d9e9ce4847ad3eb4334]; Tilotta, Sally (NIH/NIEHS) [E] [/O=NIH/OU=EXTernal (FYDIBOHF25SPDLT)/cn=Recipients/cn=8a8f652ee61f49ba9406360a95e982eb]; Walker, Robert (NIH/NIAMS) [E] [/O=NIH/OU=Nihexchange/cn=recipients/cn=walkerrobert]; Wong, Jennifer (NIH/NIMH) [E] [/O=NIH/OU=NIHEXCHANGE/cn=Recipients/cn=wongje]; Wood, Fred (NIH/NLM) [E] [/O=NIH/OU=NIHEXCHANGE/cn=NLM/cn=fredwood]; Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]

Subject: FYI: Knowledge Ecology International Update

Consumer Group Tries Again To Assert March-In Rights On Cancer Treatment Xtandi.

STAT (4/19, Silverman) reports that the consumer group Knowledge Ecology International is asking the Trump Administration to assert so-called march-in rights on the prostate cancer treatment Xtandi, which is marketed by Astellas Pharma at a wholesale cost of $129,000 per year. The group said in a letter that the drug was developed with grants from the National Institutes of Health and the Department of Defense by the University of California, Los Angeles, which went on to license the treatment. STAT says that the group first asked the Obama Administration to use march-in rights on the drug, but it "is betting its effort will have a greater chance of appealing to President Trump."

Anna Z. Amar
Senior Intellectual Property Advisor
Office of the Director
Division of Cancer Treatment and Diagnosis
National Cancer Institute
National Institutes of Health
Room 4W454, 9609 Medical Center Dr.
Rockville, MD 20850-9732
Ph: 240-276-5529
aa54d@nih.gov

From: Freel, Rose (NIH/NCI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=E8AE9AAB7E3249E881BB573E9A189036-FREELRM]
Sent: 7/19/2018 6:57:22 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
CC: Rodriguez, Richard (NIH/NCI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8092cb5394e04733ac0d4d84d25f65e5-rodrigr]; Berkley, Dale (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5ee461c29f5045a49f0adf82caaa2f31-berkleyd]
Subject: RE: Prospective Grant of an Exclusive Patent License: Development of an Anti-Mesothelin Chimeric Antigen Receptor (CAR) for the Treatment of Human Cancer to Atara Biotherapeutics Inc.

Okay, thank you both! I will come up with a response and send to you both for review before sending.

Best,
Rose

--
Rose Santangelo Freel, Ph.D.
Senior Technology Transfer Manager
National Cancer Institute
P 301-624-1257 | rose.freel@nih.gov

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Thursday, July 19, 2018 2:55 PM
To: Freel, Rose (NIH/NCI) [E] <rose.freel@nih.gov>
Cc: Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>; Berkley, Dale (NIH/OD) [E] <BerkleyD@OD.NIH.GOV>
Subject: RE: Prospective Grant of an Exclusive Patent License: Development of an Anti-Mesothelin Chimeric Antigen Receptor (CAR) for the Treatment of Human Cancer to Atara Biotherapeutics Inc.

I agree with Dale with a suggestion. **b5**
b5

From: Freel, Rose (NIH/NCI) [E]
Sent: Thursday, July 19, 2018 8:05 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Cc: Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>; Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>
Subject: RE: Prospective Grant of an Exclusive Patent License: Development of an Anti-Mesothelin Chimeric Antigen Receptor (CAR) for the Treatment of Human Cancer to Atara Biotherapeutics Inc.

Hi Mark,

Just following up on this, let me know your thoughts on a response to KEI.

Thanks!
Rose

--
Rose Santangelo Freel, Ph.D.
Senior Technology Transfer Manager
National Cancer Institute
P 301-624-1257 | rose.freel@nih.gov

From: Freel, Rose (NIH/NCI) [E]
Sent: Tuesday, July 17, 2018 8:11 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Cc: Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>; Berkley, Dale (NIH/OD) [E] <BerkleyD@OD.NIH.GOV>
Subject: FW: Prospective Grant of an Exclusive Patent License: Development of an Anti-Mesothelin Chimeric Antigen Receptor (CAR) for the Treatment of Human Cancer to Atara Biotherapeutics Inc.

Hi Mark,

Attached are comments I received from KEI on the FR Notice for the Prospective Grant to Atara. Can you please tell me if and how we should respond?

Thanks!
Rose

--
Rose Santangelo Freel, Ph.D.
Senior Technology Transfer Manager
National Cancer Institute
P 301-624-1257 | rose.freel@nih.gov

From: James Love <james.love@keionline.org>
Sent: Friday, July 13, 2018 4:45 PM
To: Freel, Rose (NIH/NCI) [E] <rose.freel@nih.gov>
Cc: Tim Reed <Tim@haiweb.org>; Luis Gil Abinader <luis.gil.abinader@keionline.org>; Merith Basey <merith@essentialmedicine.org>; Alex Lawson <alawson@socialsecurityworks.org>; Fran Quigley b6; Baker, Brook <b.baker@northeastern.edu>; Meg Jones-Monteiro <mjonesmonteiro@iccr.org>; Manon Ress <MANON.RESS@cancerunion.org>; Claire Cassedy <claire.cassedy@keionline.org>; Thiru Balasubramaniam <thiru@keionline.org>
Subject: Re: Prospective Grant of an Exclusive Patent License: Development of an Anti-Mesothelin Chimeric Antigen Receptor (CAR) for the Treatment of Human Cancer to Atara Biotherapeutics Inc.

Dear Dr. Freel,

I'm attaching a corrected copy of the comments. The difference was just the spelling of CFR, which had been transposed in the earlier version.

Jamie

On Fri, Jul 13, 2018 at 4:09 PM, James Love <james.love@keionline.org> wrote:

> Dr. Freel,
>
> Attached are comments on the Atara license from:
>
> Health Action International (HAI)
> Health GAP
> Interfaith Center on Corporate Responsibility (ICCR)
> Knowledge Ecology International (KEI)
> People of Faith for Access to Medicines (PFAM)
> Social Security Works (SSW)
> Union for Affordable Cancer Treatment (UACT)

Universities Allied for Essential Medicines (UAEM)

--
James Love. Knowledge Ecology International
http://www.keionline.org/donate.html
KEI DC tel: +1.202.332.2670, US Mobile: +1.202.361.3040, Geneva Mobile: +41.76.413.6584, twitter.com/jamie_love

--
James Love. Knowledge Ecology International
http://www.keionline.org/donate.html
KEI DC tel: +1.202.332.2670, US Mobile: +1.202.361.3040, Geneva Mobile: +41.76.413.6584, twitter.com/jamie_love

---

From: Berkley, Dale (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/CN=OD/CN=BERKLEYD]
Sent: 4/8/2016 9:27:09 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]
Subject: RE: Objection to exclusive license to AestasRx Inc.

Thanks Mark.

Dale D. Berkley, Ph.D., J.D.
Office of the General Counsel, PHD, NIH Branch
Bldg. 31, Rm. 47
Bethesda, MD 20892
301-496-6043
301-402-2528(Fax)
This message is intended for the exclusive use of the recipient(s) named above. It may contain information that is PROTECTED or PRIVILEGED, and it should not be disseminated, distributed, or copied to persons not authorized to receive such information.

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Friday, April 08, 2016 4:55 PM
To: Berkley, Dale (NIH/OD) [E] <BerkleyD@OD.NIH.GOV>
Subject: FW: Objection to exclusive license to AestasRx Inc.

b5

From: Ano, Susan (NIH/NINDS) [E]
Sent: Friday, April 08, 2016 4:35 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Subject: FW: Objection to exclusive license to AestasRx Inc.

As requested. b5

Best regards,

Sue

Susan Ano, Ph.D.
Technology Development Coordinator
Office of Technology Transfer
The National Institute of Neurological Disorders and Stroke
The National Institutes of Health
Mail address: 31 Center Drive, Suite 8A52, MS2540
Bethesda, MD 20892
Physical location: Bldg. 31, 8A07
phone (301) 435-5515
cell b6

NIH National Institute of
Neurological Disorders
and Stroke

Have patience. All things are difficult before they become easy."
-- Saadi, poet

The attached information may be confidential. It is intended only for the addressee(s) identified above. If you are not the addressee(s), or an employee or agent of the addressee(s), please note that any dissemination, distribution, or copying of this communication is strictly prohibited. If you have received this email in error, please destroy the document and notify the sender of the error. Thank you.

From: jamespackardlove@gmail.com [mailto:jamespackardlove@gmail.com] **On Behalf Of** Jamie Love
Sent: Friday, April 08, 2016 3:10 PM
To: Ano, Susan (NIH/NINDS) [E] <susan.ano@nih.gov>
Subject: Objection to exclusive license to AestasRx Inc.

Susan Ano, Ph.D., NINDS Technology Transfer,
31 Center Drive, Suite 8A52, MSC2540
Bethesda, MD 20892;
Telephone: (301) 435-5515;
anos@mail.nih.gov

Dear Dr. Ano,

I am writing to express our objection to the grant of an exclusive license

to AestasRx Inc., for patents related to the technologies noticed in the federal register under this title:

Prospective Grant of Start-up Exclusive License: Therapeutics and PMA-Approved Diagnostics for Alzheimer's Disease (intranasal delivery), Parkinson's Disease, Neuropathy,Neuropathic Pain, Peripheral Neuropathy, Diabetic Neuropathy, Neurapraxia, Axonotmesis and Neurotmesis
https://federalregister.gov/a/2016-08097

Before the NIH issues any license to AestasRx Inc. for these technologies, we request the NIH to provide the public with evidence of the following:

1. That the NIH has determined an an exclusive license is necessary for the development of the patented inventions, and there exists a written analysis which establishes that this evaluation has been done.

2. That the scope of the exclusive rights meet the requirement of 404.7(a)(1)(ii)(D), that

"The proposed terms and scope of exclusivity are not greater than reasonably necessary to provide the incentive for bringing the invention to practical application or otherwise promote the invention's utilization by the public;"

In this regard, please provide KEI with any economic analysis if any that was used to determine the number of years of exclusivity to be licensed, or to evaluate any other terms relevant to the licenses terms and scope of exclusivity.

3. That the license provides sufficient assurances that U.S. consumers will not pay more than consumers in other high income countries, and that the products based upon the patented invention will be available at affordable prices in the United States, and at affordable prices in developing countries.

KEI also requests under the Freedom of Information Act (FOIA) all correspondence, commentary and analysis of the proposed exclusive licensing from all parties within and outside of the government.

We (KEI) waives all objections to releasing this communication under FOIA.

Sincerely,

James Love
Director
Knowledge Ecology International
1621 Connecticut Avenue, Suite 500
Washington, DC 20009

James.Love@keionline.org
http://keionline.org

--
James Love. Knowledge Ecology International
http://www.keionline.org/donate.html
KEI DC tel: +1.202.332.2670, US Mobile: +1.202.361.3040, Geneva Mobile: +41.76.413.6584,
twitter.com/jamie_love

From: Joe Allen [jallen@allen-assoc.com]
Sent: 4/24/2017 9:40:48 PM
To: Stevens, Ashley J [astevens@bu.edu]; Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]; Robert Hardy [rhardy@cogr.edu]
Subject: Re: Fwd.: Army rejects request to deny Sanofi an exclusive license for a Zika vaccine

You trained him well. Now he's added to the growing list of those incurring Jaime's wrath.

Not related to tech transfer, but if you've ever been to Rio you will appreciate this: https://www.youtube-nocookie.com/embed/VxlKZereog0?rel=0

On 4/24/2017 5:37 PM, Stevens, Ashley J wrote:

> Barry Datloff worked for me 25 years ago at Dana-Farber!
>
> Best wishes,
>
> Ashley Stevens
> Focus IP Group, LLC
> Winchester, MA
>
> Office: (781) 721-2670
> Cell: b6
>
> **From:** Joe Allen [mailto:jallen@allen-assoc.com]
> **Sent:** Monday, April 24, 2017 5:23 PM
> **To:** Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>; Stevens, Ashley J <astevens@bu.edu>; Robert Hardy <rhardy@cogr.edu>
> **Subject:** Re: Fwd: Army rejects request to deny Sanofi an exclusive license for a Zika vaccine
>
> Best news of the day, thanks!
>
> On 4/24/2017 5:22 PM, Rohrbaugh, Mark (NIH/OD) [E] wrote:
>
>> Sent from my iPhone
>>
>> https://www.statnews.com/pharmalot/2017/04/24/army-sanofi-zika-vaccine-exclusive-license/

Army rejects request to deny Sanofi an exclusive license for a Zika vaccine

By ED SILVERMAN | APRIL 24, 2017

The US Army is proceeding with plans to grant Sanofi Pasteur an exclusive license to develop a vaccine for the Zika virus, despite concerns among some lawmakers and advocacy groups that the product may be priced too high for many Americans, even though it was developed with taxpayer funds.

In explaining its decision, an Army official wrote in a recent letter to one of the advocacy groups that the Army "lacks the means, expertise, and authority to define, implement, and enforce 'affordable prices' or to set price controls for a potential vaccine that will require great investment and face high risk of failure." Citing confidentiality, the official declined to reveal specifics of the deal.

The rebuff comes after the military last December revealed plans to award the drug maker a license to a pair of government patents. That followed months of mounting alarm among public health officials over the spread of Zika, the mosquito-borne virus that can cause birth defects. At the same time, there has been speculation that the market for such a vaccine could become lucrative.

Sanofi Pasteur, one of the world's biggest vaccine makers and a unit of the French drug maker, was also awarded a $43.2 million grant by the Biomedical Advanced Research and Development Authority and has a co-development deal with the Walter Reed Army Institute of Research. A Sanofi spokeswoman has previously said the company expects to seek more BARDA funding.

Over the past few months, nearly a dozen congressional Democrats and several advocacy groups urged the Army to reject an exclusive license. Alternatively, they argued the Army should, instead, issue a limited license and impose requirements allowing the federal government to intervene if the company sets a price that would make the vaccine inaccessible to many Americans.

Last month, Sen. Bernie Sanders (I-Vt.) drew attention to the issue by writing in The New York Times that if, the Trump administration "allows this deal, Sanofi will be able to charge whatever astronomical price it wants for its vaccine… American consumers should not be forced to pay the highest price in the world for a vaccine we paid to help develop."

Meanwhile, Knowledge Ecology International and other groups asked the Army Medical Research and Materiel Command for information about the terms, such as how long the license would run, how much the government has spent, royalty rates, and pricing. The advocacy group made a point of citing federal law indicating exclusive licensing should be made only to serve a public benefit.

In response, Barry Datlof, the director of medical technology transfer at the Medical Research and Materiel Command, wrote that any exclusive license will be awarded in the "best interest of the US government and the public, and it will be a reasonable and necessary incentive" to harness the capital and expertise to win FDA approval for an "unproven technology."

He added that, "granting an exclusive license under our existing technology transfer framework, an exclusive license places restrictions and requirements upon the licensee [which is Sanofi] that are designed to protect the public interest." We wrote him to ask for information about the "restrictions and requirements" and will pass along any reply.

Datlof added that limiting an exclusive license to five years would not be "sufficient to attract quality partners." Granting an exclusive license for a federally developed technology is "often the only incentive significant enough to attractive a competent and willing commercial partner." He also maintained Sanofi was the only company interested in pursuing a collaborative research agreement.

One advocacy group was livid.

"The Trump administration is proposing that for a vaccine, invented by the Army and funded by the National Institutes of Health, a French company, can charge whatever it wants in the US, even if that is twice or three times what other countries pay," said Jamie Love of Knowledge Ecology International, who received the letter.

"The 'charge whatever you want' policy is a 'kick me' sign we will attach to ourselves," Love said. "This is a good outcome for the French drug company and a bad outcome for anyone in the US who will want the vaccine, or pay for it through taxes and insurance premiums."

--

Joseph P. Allen
President
Allen and Associates
60704 Rt. 26, South
Bethesda, OH 43719
(W) 740-484-1814
(c) b6
www.allen-assoc.com

--

Joseph P. Allen
President
Allen and Associates
60704 Rt. 26, South
Bethesda, OH 43719
(W) 740-484-1814
(c) b6
www.allen-assoc.com

From: Vepa, Sury (NIH/NCATS) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=25B6C29F123544738FCBAD51627B2D23-VEPAS]
Sent: 7/19/2018 2:59:24 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Portilla, Lili (NIH/NCATS) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=9b03f548be224eb9b7b6167a32e9cc4a-portilll]
Subject: FW: Prospective Grant of Exclusive Patent License: Mutant IDH1 Inhibitors Useful for Treating Cancer to Apexx Oncology. Notice for comment published in 83 FR 29562.

Hi Mark and Lili,

Please see below a draft response email to KEI. My responses are based on responses previously provided by NCI and NIAID. Would appreciate your suggestions before I send them to KEI.

Thanks,

Sury

b5

b5

Sury

Phone: 301-827-7181
Cell: b6
E-Mail: sury.vepa@nih.gov

From: James Love [mailto:james.love@keionline.org]
Sent: Tuesday, July 10, 2018 4:35 PM
To: Vepa, Sury (NIH/NCATS) [E] <sury.vepa@nih.gov>
Cc: Luis Gil Abinader <luis.gil.abinader@keionline.org>; Claire Cassedy <claire.cassedy@keionline.org>; Manon Ress <manon.ress@keionline.org>; Thiru Balasubramaniam <thiru@keionline.org>
Subject: Re: Prospective Grant of Exclusive Patent License: Mutant IDH1 Inhibitors Useful for Treating Cancer to Apexx Oncology. Notice for comment published in 83 FR 29562.

July 10, 2018

Sury Vepa, Ph.D., J.D.,
Senior Licensing and Patenting Manager,
National Center for Advancing Translational Sciences
National Institutes of Health
Email sury.vepa@nih.gov

Re: Prospective Grant of Exclusive Patent License: Mutant IDH1 Inhibitors Useful for Treating Cancer to Apexx Oncology. Notice for comment published in 83 FR 29562.

https://www.federalregister.gov/documents/2018/06/25/2018-13486/prospective-grant-of-exclusive-patent-license-mutant-idh1-inhibitors-useful-for-treating-cancer

Dear Dr. Vepa,

Knowledge Ecology International (KEI) offers the following comments on the, “Prospective Grant of Exclusive Patent License: Mutant IDH1 Inhibitors Useful for Treating Cancer,” to Apexx Oncology, which was noticed in the Federal Register (83 FR 29562).

As far as the public can determine, Apexx Oncology is a secretive startup company. The only information we could find using a Google search about the company was a contest for a logo of the company. There is no record of a registered trademark for Apexx Oncology with the USPTO. No web page has been located. It is not obvious if Apexx Oncology is a new name for GeneXion Oncology (as indicated today), or a new company entirely, and in any case, there is next to nothing generally known about the company under either name.

When the NIH proposes giving an exclusive license on a patent to a company for which almost nothing is known, it should provide at the very least some basic information about the company. In seeking to respond to the first FR notice in this case, we had asked if GeneXion was owned by a company in Switzerland, but the NIH declined to answer. We don't know who is on the board of directors, who the key staff are or if another company owns this company. We would like to know if any current or former NIH employees or contractors are part of the company.

We also seek to learn -- why this company was selected in the first place? Do they have people who have worked on this particular technology, or have some special expertise? And since the patents are fairly new, did the NIH have no reasonable prospects for a license to an entity with more resources and a stronger track record than a company that seems to barely exist?

Here are some general provisions that we recommend for an exclusive license by the NIH.

1. **No discrimination against US residents in pricing.**

Prices in the U.S. for any drug, vaccine, medical device or other health technology using the invention should not be higher than the median price charged in the seven countries with the largest gross domestic product (GDP), that also have a per capita income of at least 50 percent of the United States, as measured by the World Bank Atlas Method.

2. **Developing countries.**

The license should not be exclusive for countries with a per capita income that is less than 30 percent of the US.

3. **Transparency.**

The licensee should be required to file an annual report to the NIH, available to the public, on the research and development (R&D) costs associated with the development of any product that uses the invention, including reporting separately and individually the outlays on each clinical trial. We will note that this is not a request to see a company business plan or license application. We are asking that going forward the company be required to report on actual R&D outlays to develop the subject inventions.

4. **Reduce term of exclusivity when revenues are large.**

The exclusivity of the license in the U.S. should be reduced by one year for every $500 million in revenue equivalents, earned after the first $1 billion, where revenue equivalent is defined as global cumulative sales plus market entry rewards as well as government grants or tax credits, for the product or products using the invention.

Sincerely,

James Love
Knowledge Ecology International
james.love@keionline.org
https://keionline.org

--
James Love. Knowledge Ecology International
http://www.keionline.org/donate.html
KEI DC tel: +1.202.332.2670, US Mobile: +1.202.361.3040, Geneva Mobile: +41.76.413.6584,
twitter.com/jamie_love

From: Myles, Renate (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/CN=RECIPIENTS/CN=MYLESR]
Sent: 4/24/2017 9:41:20 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]
Subject: RE: Army rejects request to deny Sanofi an exclusive license for a Zika vaccine

Shall I share with executive committee?

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, April 24, 2017 5:35 PM
To: Gottesman, Michael (NIH/OD) [E] <GottesmM@mail.nih.gov>; Myles, Renate (NIH/OD) [E] <mylesr@od.nih.gov>; Kleinman, Joe (NIH/OD) [E] <kleinmanj@od.nih.gov>; Wyatt, Richard G (NIH/OD) [E] <WyattRG@OD.NIH.GOV>; McGarey, Barbara (NIH/OD) [E] <MCGAREYB@od.nih.gov>; McBurney, Margaret (NIH/OD) [E] <mmcburney@od.nih.gov>; Berkley, Dale (NIH/OD) [E] <BerkleyD@OD.NIH.GOV>; Garcia-Perez, Arlyn (NIH/OD) [E] <GarciaA@OD.NIH.GOV>; Wanjek, Christopher (NIH/OD) [E] <wanjekc@od.nih.gov>
Subject: FW: Army rejects request to deny Sanofi an exclusive license for a Zika vaccine

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, April 24, 2017 5:22 PM
To: ashley stevens <astevens@bu.edu>; Robert Hardy <rhardy@cogr.edu>; Joseph Allen <jallen@allen-assoc.com>
Subject: Fwd: Army rejects request to deny Sanofi an exclusive license for a Zika vaccine

Sent from my iPhone

https://www.statnews.com/pharmalot/2017/04/24/army-sanofi-zika-vaccine-exclusive-license/

Army rejects request to deny Sanofi an exclusive license for a Zika vaccine

By ED SILVERMAN | APRIL 24, 2017

The US Army is proceeding with plans to grant Sanofi Pasteur an exclusive license to develop a vaccine for the Zika virus, despite concerns among some lawmakers and advocacy groups that the product may be priced too high for many Americans, even though it was developed with taxpayer funds.

In explaining its decision, an Army official wrote in a recent letter to one of the advocacy groups that the Army "lacks the means, expertise, and authority to define, implement, and enforce 'affordable prices' or to set price controls for a potential vaccine that will require great investment and face high risk of failure." Citing confidentiality, the official declined to reveal specifics of the deal.

The rebuff comes after the military last December revealed plans to award the drug maker a license to a pair of government patents. That followed months of mounting alarm among public health officials over the spread of Zika, the mosquito-borne virus that can cause birth defects. At the same time, there has been speculation that the market for such a vaccine could become lucrative.

Sanofi Pasteur, one of the world's biggest vaccine makers and a unit of the French drug maker, was also awarded a $43.2 million grant by the Biomedical Advanced Research and Development Authority and has a co-development deal with the Walter Reed Army Institute of Research. A Sanofi spokeswoman has previously said the company expects to seek more BARDA funding.

Over the past few months, nearly a dozen congressional Democrats and several advocacy groups urged the Army to reject an exclusive license. Alternatively, they argued the Army should, instead, issue a limited license and impose requirements allowing the federal government to intervene if the company sets a price that would make the vaccine inaccessible to many Americans.

Last month, Sen. Bernie Sanders (I-Vt.) drew attention to the issue by writing in The New York Times that if, the Trump administration "allows this deal, Sanofi will be able to charge whatever astronomical price it wants for its vaccine… American consumers should not be forced to pay the highest price in the world for a vaccine we paid to help develop."

Meanwhile, Knowledge Ecology International and other groups asked the Army Medical Research and Materiel Command for information about the terms, such as how long the license would run, how much the government has spent, royalty rates, and pricing. The advocacy group made a point of citing federal law indicating exclusive licensing should be made only to serve a public benefit.

In response, Barry Datlof, the director of medical technology transfer at the Medical Research and Materiel Command, wrote that any exclusive license will be awarded in the "best interest of the US government and the public, and it will be a reasonable and necessary incentive" to harness the capital and expertise to win FDA approval for an "unproven technology."

He added that, "granting an exclusive license under our existing technology transfer framework, an exclusive license places restrictions and requirements upon the licensee [which is Sanofi] that are designed to protect the public interest." We wrote him to ask for information about the "restrictions and requirements" and will pass along any reply.

Datlof added that limiting an exclusive license to five years would not be "sufficient to attract quality partners." Granting an exclusive license for a federally developed technology is "often the only incentive significant enough to attractive a competent and willing commercial partner." He also maintained Sanofi was the only company interested in pursuing a collaborative research agreement.

One advocacy group was livid.

"The Trump administration is proposing that for a vaccine, invented by the Army and funded by the National Institutes of Health, a French company, can charge whatever it wants in the US, even if that is twice or three times what other countries pay," said Jamie Love of Knowledge Ecology International, who received the letter.

"The 'charge whatever you want' policy is a 'kick me' sign we will attach to ourselves," Love said. "This is a good outcome for the French drug company and a bad outcome for anyone in the US who will want the vaccine, or pay for it through taxes and insurance premiums."

From: Berkley, Dale (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=5EE461C29F5045A49F0ADF82CAAA2F31-BERKLEYD]
Sent: 7/19/2018 1:30:48 PM
To: Freel, Rose (NIH/NCI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e8ae9aab7e3249e881bb573e9a189036-freelrm]; Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
CC: Rodriguez, Richard (NIH/NCI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8092cb5394e04733ac0d4d84d25f65e5-rodrigr]
Subject: RE: Prospective Grant of an Exclusive Patent License: Development of an Anti-Mesothelin Chimeric Antigen Receptor (CAR) for the Treatment of Human Cancer to Atara Biotherapeutics Inc.

Rose—just one comment from me. b5

b5

Best, Dale

Dale D. Berkley, Ph.D., J.D.
Office of the General Counsel, PHD, NIH Branch
Bldg. 31, Rm. 47
Bethesda, MD 20892
301-496-6043
301-402-2528(Fax)

This message is intended for the exclusive use of the recipient(s) named above. It may contain information that is PROTECTED or PRIVILEGED, and it should not be disseminated, distributed, or copied to persons not authorized to receive such information.

From: Freel, Rose (NIH/NCI) [E]
Sent: Thursday, July 19, 2018 8:05 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Cc: Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>; Berkley, Dale (NIH/OD) [E] <berkleyd@od.nih.gov>
Subject: RE: Prospective Grant of an Exclusive Patent License: Development of an Anti-Mesothelin Chimeric Antigen Receptor (CAR) for the Treatment of Human Cancer to Atara Biotherapeutics Inc.

Hi Mark,

Just following up on this, let me know your thoughts on a response to KEI.

Thanks!
Rose

--
Rose Santangelo Freel, Ph.D.
Senior Technology Transfer Manager
National Cancer Institute
P 301-624-1257 | rose.freel@nih.gov

From: Freel, Rose (NIH/NCI) [E]
Sent: Tuesday, July 17, 2018 8:11 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Cc: Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>; Berkley, Dale (NIH/OD) [E] <BerkleyD@OD.NIH.GOV>
Subject: FW: Prospective Grant of an Exclusive Patent License: Development of an Anti-Mesothelin Chimeric Antigen Receptor (CAR) for the Treatment of Human Cancer to Atara Biotherapeutics Inc.

Hi Mark,

Attached are comments I received from KEI on the FR Notice for the Prospective Grant to Atara. Can you please tell me if and how we should respond?

Thanks!
Rose

--
Rose Santangelo Freel, Ph.D.
Senior Technology Transfer Manager
National Cancer Institute
P 301-624-1257 | rose.freel@nih.gov

From: James Love <james.love@keionline.org>
Sent: Friday, July 13, 2018 4:45 PM
To: Freel, Rose (NIH/NCI) [E] <rose.freel@nih.gov>
Cc: Tim Reed <Tim@haiweb.org>; Luis Gil Abinader <luis.gil.abinader@keionline.org>; Merith Basey <merith@essentialmedicine.org>; Alex Lawson <alawson@socialsecurityworks.org>; Fran Quigley b6; Baker, Brook <b.baker@northeastern.edu>; Meg Jones-Monteiro <mjonesmonteiro@iccr.org>; Manon Ress <MANON.RESS@cancerunion.org>; Claire Cassedy <claire.cassedy@keionline.org>; Thiru Balasubramaniam <thiru@keionline.org>
Subject: Re: Prospective Grant of an Exclusive Patent License: Development of an Anti-Mesothelin Chimeric Antigen Receptor (CAR) for the Treatment of Human Cancer to Atara Biotherapeutics Inc.

Dear Dr. Freel,

I'm attaching a corrected copy of the comments. The difference was just the spelling of CFR, which had been transposed in the earlier version.

Jamie

On Fri, Jul 13, 2018 at 4:09 PM, James Love <james.love@keionline.org> wrote:

> Dr. Freel,
>
> Attached are comments on the Atara license from:
>
> Health Action International (HAI)
> Health GAP
> Interfaith Center on Corporate Responsibility (ICCR)
> Knowledge Ecology International (KEI)
> People of Faith for Access to Medicines (PFAM)
> Social Security Works (SSW)
> Union for Affordable Cancer Treatment (UACT)
> Universities Allied for Essential Medicines (UAEM)
>
> --
> James Love. Knowledge Ecology International
> http://www.keionline.org/donate.html
> KEI DC tel: +1.202.332.2670, US Mobile: +1.202.361.3040, Geneva Mobile: +41.76.413.6584, twitter.com/jamie_love

--
James Love. Knowledge Ecology International
http://www.keionline.org/donate.html
KEI DC tel: +1.202.332.2670, US Mobile: +1.202.361.3040, Geneva Mobile: +41.76.413.6584, twitter.com/jamie_love

From: Stevens, Ashley J [astevens@bu.edu]
Sent: 4/24/2017 9:37:42 PM
To: Joe Allen [jallen@allen-assoc.com]; Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]; Robert Hardy [rhardy@cogr.edu]
Subject: RE: Fwd.: Army rejects request to deny Sanofi an exclusive license for a Zika vaccine

Barry Datloff worked for me 25 years ago at Dana-Farber!

Best wishes,

Ashley Stevens
Focus IP Group, LLC
Winchester, MA

Office: (781) 721-2670
Cell: b6

From: Joe Allen [mailto:jallen@allen-assoc.com]
Sent: Monday, April 24, 2017 5:23 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>; Stevens, Ashley J <astevens@bu.edu>; Robert Hardy <rhardy@cogr.edu>
Subject: Re: Fwd: Army rejects request to deny Sanofi an exclusive license for a Zika vaccine

Best news of the day, thanks!

On 4/24/2017 5:22 PM, Rohrbaugh, Mark (NIH/OD) [E] wrote:

> Sent from my iPhone
>
> https://www.statnews.com/pharmalot/2017/04/24/army-sanofi-zika-vaccine-exclusive-license/
>
> # Army rejects request to deny Sanofi an exclusive license for a Zika vaccine
>
> By ED SILVERMAN | APRIL 24, 2017

The US Army is proceeding with plans to grant Sanofi Pasteur an exclusive license to develop a vaccine for the Zika virus, despite concerns among some lawmakers and advocacy groups that the product may be priced too high for many Americans, even though it was developed with taxpayer funds.

In explaining its decision, an Army official wrote in a recent letter to one of the advocacy groups that the Army "lacks the means, expertise, and authority to define, implement, and enforce 'affordable prices' or to set price controls for a potential vaccine that will require great investment and face high risk of failure." Citing confidentiality, the official declined to reveal specifics of the deal.

The rebuff comes after the military last December revealed plans to award the drug maker a license to a pair of government patents. That followed months of mounting alarm among public health officials over the spread of Zika, the mosquito-borne virus that can cause birth defects. At the same time, there has been speculation that the market for such a vaccine could become lucrative.

Sanofi Pasteur, one of the world's biggest vaccine makers and a unit of the French drug maker, was also awarded a $43.2 million grant by the Biomedical Advanced Research and Development Authority and has a co-development deal with the Walter Reed Army Institute of Research. A Sanofi spokeswoman has previously said the company expects to seek more BARDA funding.

Over the past few months, nearly a dozen congressional Democrats and several advocacy groups urged the Army to reject an exclusive license. Alternatively, they argued the Army should, instead, issue a limited license and impose requirements allowing the federal government to intervene if the company sets a price that would make the vaccine inaccessible to many Americans.

Last month, Sen. Bernie Sanders (I-Vt.) drew attention to the issue by writing in The New York Times that if, the Trump administration "allows this deal, Sanofi will be able to charge whatever astronomical price it wants for its vaccine… American consumers should not be forced to pay the highest price in the world for a vaccine we paid to help develop."

Meanwhile, Knowledge Ecology International and other groups asked the Army Medical Research and Materiel Command for information about the terms, such as how long the license would run, how much the government has spent, royalty rates, and pricing. The advocacy group made a point of citing federal law indicating exclusive licensing should be made only to serve a public benefit.

In response, Barry Datlof, the director of medical technology transfer at the Medical Research and Materiel Command, wrote that any exclusive license will be awarded in the “best interest of the US government and the public, and it will be a reasonable and necessary incentive” to harness the capital and expertise to win FDA approval for an “unproven technology.”

He added that, “granting an exclusive license under our existing technology transfer framework, an exclusive license places restrictions and requirements upon the licensee [which is Sanofi] that are designed to protect the public interest.” We wrote him to ask for information about the “restrictions and requirements” and will pass along any reply.

Datlof added that limiting an exclusive license to five years would not be “sufficient to attract quality partners.” Granting an exclusive license for a federally developed technology is “often the only incentive significant enough to attractive a competent and willing commercial partner.” He also maintained Sanofi was the only company interested in pursuing a collaborative research agreement.

One advocacy group was livid.

“The Trump administration is proposing that for a vaccine, invented by the Army and funded by the National Institutes of Health, a French company, can charge whatever it wants in the US, even if that is twice or three times what other countries pay,” said Jamie Love of Knowledge Ecology International, who received the letter.

“The ‘charge whatever you want’ policy is a ‘kick me’ sign we will attach to ourselves,” Love said. “This is a good outcome for the French drug company and a bad outcome for anyone in the US who will want the vaccine, or pay for it through taxes and insurance premiums.”

--

Joseph P. Allen
President
Allen and Associates
60704 Rt. 26, South
Bethesda, OH 43719
(W) 740-484-1814
(c) b6
www.allen-assoc.com

From: Shmilovich, Michael (NIH/NHLBI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7DFE19BFD1D443CEB700B9F22D159A90-SHMILOVM]
Sent: 8/31/2018 2:45:46 AM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Berkley, Dale (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5ee461c29f5045a49f0adf82caaa2f31-berkleyd]; Deutch, Alan (NIH/NHLBI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=244d755700584812af36b5e787285647-deutcha]
Subject: NIH to KEI re Inversago T1D 30Aug2018.docx
Attachments: NIH to KEI re Inversago T1D 30Aug2018.docx

Take 2 on Inversago response. Slightly condensed. Please review and advise.

Thank you all!

b5

From: Joe Allen [jallen@allen-assoc.com]
Sent: 12/20/2016 8:13:31 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]; Robert Hardy [rhardy@cogr.edu]; Hammersla, Ann (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=Recipients/cn=hammerslaa]
Subject: Re: Fwd: NYT: Harnessing the U.S. Taxpayer to Fight Cancer and Make Profits

Thanks, think I'm going to reply to this and last week's piece lauding price controls march in's. If you have any data points on the CRADA or other allegations to help refute the article, please pass them along.

On 12/20/2016 12:29 PM, Rohrbaugh, Mark (NIH/OD) [E] wrote:

> I did. The biggest problem is that they did not even balance their statements that we have the right to control prices, intra and extramurally, except they note our experience with the reasonable pricing clause. They speak to the same "experts" without noting other important and more influential points of view.
>
> **From:** Joe Allen [mailto:jallen@allen-assoc.com]
> **Sent:** Tuesday, December 20, 2016 9:39 AM
> **To:** Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>; Robert Hardy <rhardy@cogr.edu>; Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
> **Subject:** Re: Fwd: NYT: Harnessing the U.S. Taxpayer to Fight Cancer and Make Profits
>
> you might pass this along to Ashley who was asking if Andrew Pollack was involved in last week's anti Bayh-Dole article. He wasn't but sure had his fingerprints on this one.
>
> On 12/19/2016 8:57 PM, Rohrbaugh, Mark (NIH/OD) [E] wrote:
>
> Sent from
>
> **Health**
>
> # Harnessing the U.S. Taxpayer to Fight Cancer and Make Profits
>
> By MATT RICHTEL and ANDREW POLLACK DEC. 19, 2016

Dr. Steven Rosenberg, left, who has led the surgery branch at the National Cancer Institute for 42 years, and Dr. Arie Belldegrun, the founder of Kite Pharma. Credit Jesse Dittmar (left) and Emily Berl (right) for The New York Times

Enthusiasm for cancer immunotherapy is soaring, and so is Arie Belldegrun's fortune.

Dr. Belldegrun, a physician, co-founded Kite Pharma, a company that could be the first to market next year with a highly anticipated new immunotherapy treatment. But even without a product, Dr. Belldegrun has struck gold.

His stock in Kite is worth about $170 million. Investors have profited along with him, as the company's share price has soared to about $50 from an initial price of $17 in 2014.

The results reflect widespread excitement over immunotherapy, which harnesses the body's immune system to attack cancer and has rescued some patients from near-certain death. But they also speak volumes about the value of Kite's main scientific partner: the United States government.

Kite's treatment, a form of immunotherapy called CAR-T, was initially developed by a team of researchers at the National Cancer Institute, led by a longtime friend and mentor of Dr. Belldegrun. Now Kite pays several million a year to the government to support continuing research dedicated to the company's efforts.

The relationship puts American taxpayers squarely in the middle of one of the hottest new drug markets. It also raises a question: Are taxpayers getting a good deal?

Defenders say that the partnership will likely bring a lifesaving treatment to patients, something the government cannot really do by itself, and that that is what matters most.

Critics say that taxpayers will end up paying twice for the same drug — once to support its development and a second time to buy it — while the company reaps the financial benefit.

“If this was not a government-funded cancer treatment — if it was for a new solar technology, for example — it would be scandalous to think that some private investors are reaping massive profits off a taxpayer-funded invention,” said James Love, director of Knowledge Ecology International, an advocacy group concerned with access to medicines.

Photo

Dr. Rosenberg and Dr. Belldegrun in the mid-1980s. Dr. Belldegrun became a research fellow for Dr. Rosenberg at the cancer institute in 1985. Credit Kite Pharma

The debate goes squarely to one of the nation’s most vexing challenges: rising health care and drug prices. Kite is one of a growing number of drug and biotech companies relying on federal laboratories. Analysts expect the company to charge at least $200,000 for the new treatment, which is intended as a one-time therapy for patients.

While the law allows the government to demand drug-price concessions from its private-sector partners, the government has declined to do so with Kite and generally disdains the practice. Insisting on lower prices, federal researchers say, would drive away innovative partners that speed the drug-development process and benefit patients. But with the government doing so much pivotal research, others say that the private sector cannot afford to walk away.

“The market is so reliant on the knowledge and know-how that comes out of the government and academic labs,” said Dr. Aaron Kesselheim, director of the Program on Regulation, Therapeutics and Law at Brigham & Women’s Hospital in Boston.

Price curbs, he said, “would not suddenly lead to a total abandonment of this pipeline. It couldn’t possibly.”

Drug makers would be especially unlikely to turn away from immunotherapy, where the promising science has set off a “gold rush mentality,” according to Mark Edwards of Bioscience Advisors, a company which tracks pharmaceutical licensing deals.

The National Institutes of Health, the parent agency of the National Cancer Institute, currently has about 400 cooperative research agreements with companies, and licenses hundreds of patented inventions for private-sector development.

Kite executives and national health officials characterize their partnership as a model arrangement in a system established by Congress three decades ago. The system has given birth to the cancer drug Taxol, the AIDS drug Prezista, two cervical cancer vaccines and a widely used test for H.I.V. infection, among other innovations.

Continue reading the main story

Photo

Dr. Rosenberg in his lab at the cancer institute in Bethesda, Md. Partnerships between government labs and drug companies are “absolutely essential or many discoveries will not see the light of day,” he said. Credit Jesse Dittmar for The New York Times

Kite's first drug, called KTE-C19, could help thousands of patients each year in the United States with certain blood cancers. If it succeeds, it could generate sales of $1 billion to $2 billion annually, according to Wall Street analysts, making it among the most lucrative drugs to come from government research.

But the government's share of any Kite success would be modest, much lower than some academic research groups have wrangled in immunotherapy deals worth hundreds of millions of dollars. Federal officials counter that the reward to the taxpayer is not money but the drug itself.

"This is exactly the way things should work," said Dr. Steven Rosenberg, who has led the surgery branch at the National Cancer Institute for 42 years and led development of Kite's drug. Such partnerships, he said, are "absolutely essential or many discoveries will not see the light of day."

Moreover, government officials say, companies in such deals must take significant financial risks and expenditures on their own, without any guarantee that the drug will be approved.

Kite says it has spent more than $200 million on research and development, including running larger clinical trials than those conducted by the cancer institute, and recently spent about $30 million to build a factory that will be able to make treatments for up to 5,000 patients a year.

Setting the price of the drug, Dr. Rosenberg said, "is for the marketplace."

A Public-Private Partnership

Like many business deals, this one began with a personal relationship — in this case between Dr. Rosenberg and Dr. Belldegrun.

After finishing medical school in his native Israel, performing surgery in helicopters for the Israeli armed forces, and completing residency at Brigham & Women's Hospital, Dr. Belldegrun became a research fellow for Dr. Rosenberg at the N.C.I. It was 1985, and Dr. Belldegrun was put to work on a new project of Dr. Rosenberg's — extracting tumor-fighting immune cells from cancer patients, multiplying them in the laboratory, and putting them back in.

"He was one of the more outstanding fellows to come through," said Dr. Rosenberg, 76, who is widely considered a cancer research luminary.

Continue reading the main story

Photo

The linked image cannot be displayed. The file may have been moved, renamed, or deleted. Verify that the link points to the correct file and location.

Dr. Belldegrun, center, at the Nasdaq stock exchange, where Kite Pharma is listed. The company was founded in 2009 and went public in 2014. Credit Nasdaq, 2016

When the fellowship ended in 1988, Dr. Belldegrun became a prominent surgeon at the University of California, Los Angeles, but the two men stayed in touch. Eventually, Dr. Belldegrun, 67, got the entrepreneurial bug. He co-founded a biotech company, Agensys, which was acquired by a bigger company for more than $500 million. He was also involved with Cougar Biotechnology, which developed the prostate cancer drug Zytiga and was acquired by Johnson & Johnson for $1 billion in May 2009. A month later, Dr. Belldegrun formed Kite with a group of colleagues and investors to pursue cancer immunotherapy.

That same month, a Florida marine contractor named Eric Karlson, whose non-Hodgkin's lymphoma was advancing despite four prior treatments, became the first patient treated by Dr. Rosenberg with what would eventually become KTE-C19. The treatment entailed removing some of Mr. Karlson's immune system T cells from his blood, genetically engineering them to recognize and fight his cancer, multiplying the T cells to huge numbers in the laboratory and transferring them back into his body. After two such treatments, Mr. Karlson remains alive and cancer-free eight years later.

Kite initially thought it would pursue an approach to immunotherapy known as cancer vaccines, but in 2010, Dr. Belldegrun visited Dr. Rosenberg and was shown the X-rays of Mr. Karlson and of a second patient.

Dr. Belldegrun was bowled over. “I had no doubt that this is going to be a drug and, more than that, it will become a platform for multiple products,” he recalled. “We never looked back.”

Over the next two years, the National Cancer Institute worked out a deal with Kite that was signed in 2012. It was the first of eight contracts between the government and the company that generally take two forms.

In one type of contract, Kite licenses patented inventions and agrees to pay the government royalties, roughly 5 percent of sales of any commercial product arising from a particular patent. However, there is no such license specifically for KTE-C19 because the underlying treatment was not patented by the N.C.I., so royalties will be minimal.

Officials say the agency did not apply for a patent because the treatment was similar to what others had been developing. Also, at the time the treatment was first created, in 2007, immunotherapy was considered to have dim commercial prospects.

“Back then, we didn’t even think about commercial aspects,” said Dr. James N. Kochenderfer, a scientist at the agency who designed the treatment when working in Dr. Rosenberg’s group.

Under the second type of contract, known as a cooperative research and development agreement, Kite provides money to the N.C.I. to support research. Kite is now paying $3 million a year to Dr. Rosenberg’s lab and has provided $7.5 million to it in total since 2012. Based on its regulatory filings, Kite is paying $7.8 million a year for research agreements and licenses in total, with at least $4 million of that going to the cancer institute and the rest to academic or corporate partners.

The taxpayer has invested, too. Dr. Rosenberg estimated that the government has spent roughly $10 million over the years on what has become KTE-C19. He said Kite’s $3 million a year is about equal to the taxpayer funding in that area and has helped speed research.

These days, researchers from Kite and the cancer institute, typically including Dr. Rosenberg and Dr. Belldegrun, confer by conference call every other Thursday for 90 minutes. Kite employees have spent long periods at the N.C.I., learning how to manufacture the therapy and how to treat patients in advance with chemotherapy.

“We shouldn’t underestimate the value and the importance of N.I.H., not only to Kite but to the whole field of engineered T-cell therapy,” Dr. Belldegrun said. When Kite signed its first deal with the cancer agency, he said, it “tapped into six years of monumental work that they had done.”

Some immunotherapy competitors marvel at the company’s coup in tapping into the agency’s expertise. “They got 20 years of research all together in one scoop,” said Dr. Carlos Paya, chief executive of Immune Design, which is pursuing a different approach.

But government officials say few, if any, other companies were interested in the technology at the time Dr. Belldegrun came calling. Dr. Rosenberg said that before Kite, a few companies, including Johnson & Johnson, had looked at an earlier version of his technology but were wary because treatment involved processing each patient's cells.

Government-developed technology available to be licensed to companies is posted on the website of the National Institutes of Health. And when the agency intends to grant a license to a particular company, it publishes that in the Federal Register, inviting public comment and possible competing offers. Both steps were taken in the case of Kite, officials said.

Kite did not get everything the cancer institute has developed in the field. Some other companies, including Opus Bio and Bluebird Bio, got rights to some products, in part because the companies had special expertise that the agency's researchers desired. But Kite seems to have gotten the balance of them and N.C.I. technology accounts for the majority of its pipeline of possible products, though the company is diversifying.

Photo

A slide that Kite Pharma used in presentations to potential investors pointed out the company's relationship with Dr. Rosenberg.

Dr. Rosenberg professes no interest in the business side of the Kite relationship. He does not own stock in any company, even Kite, though he could get up to $150,000 a year in patent royalties if some of Kite's efforts pay off.

Dr. Belldegrun, in contrast to his mentor, has commercial flair. He is known for his sharp business suits, lives in the Bel-Air neighborhood of Los Angeles, and seems as comfortable on Wall Street or in high society as in the operating room.

Kite's relationship with the N.C.I. is an important part of its appeal to investors. In some presentations, Dr. Belldegrun has shown a photograph of himself with Dr. Rosenberg in their younger days. And he persuaded Dr. Rosenberg to speak at Kite's first big meeting for investors in June 2015, the only time he has ever spoken to Wall Street.

In emails obtained through a Freedom of Information Act request by Knowledge Ecology International, Dr. Belldegrun praised Dr. Rosenberg's talk and sent him copies of investment reports from the conference written by Wall Street analysts.

"Thank you for making the effort to come to NY," Dr. Belldegrun wrote. "I heard only raving reviews about your presence and presentation."

A 'Reasonable' Question

The reliance of private companies on government-funded research goes well beyond obvious cases like Kite. In many instances, companies work with universities or medical centers that, in turn, have been funded from the $32 billion annual budget of the National Institutes of Health.

Kite's two main competitors, Novartis and Juno Therapeutics, for instance, derived similar immunotherapy treatments largely from academic institutions, developed at least in part with government funding. Novartis has a relationship with the University of Pennsylvania, and Juno with the Memorial Sloan Kettering Cancer Center, the Fred Hutchinson Cancer Research Center and Seattle Children's Hospital.

"For the most important drugs you'll see some public-sector involvement," said Bhaven Sampat, an associate professor of health policy and management at Columbia University. He was one author of a study that found that 9 percent of all drugs approved between 1988 and 2005 were based directly on a patent held by the public sector. But 47.8 percent of the drugs relied at least indirectly on some federally funded research.

Continue reading the main story

Photo

Eric Karlson at his home on Marco Island, Fla., this month. Mr. Karlson's non-Hodgkin's lymphoma was successfully treated by Dr. Rosenberg with what would eventually become KTE-C19. Credit Scott McIntyre for The New York Times

The figures were higher for more medically important drugs: 17.4 percent had a direct public-sector patent, while 64.5 percent had at least an indirect public-sector influence.

These figures are up sharply from before the 1980s. Such partnerships and licensing deals were encouraged by the 1980 Bayh-Dole and Stevenson-Wydler Acts, and the 1986 Federal Technology Transfer Act. The laws are credited with jump-starting the biotechnology industry.

But from the beginning, some people questioned whether taxpayers were getting a bad deal.

Perhaps the best-known drug developed from a cooperative research and development agreement — the cancer drug Taxol — was the subject of several congressional hearings in the early 1990s that investigated whether the drug's maker, Bristol-Myers Squibb, charged too much and whether the government recouped enough of its investment. In the end, the pricing was left unchanged.

The N.I.H. argues that if it imposes pricing restrictions, it won't get partners. In fact, in 1995, it struck from its negotiating tactics a goal that prices be "reasonable."

"Companies will not take technologies from us if we say the government will decide in the future what the price will be," said

Mark Rohrbaugh, who ran the technology transfer office at the institutes from 2001 to 2013 and is now an adviser to the agency. After the “reasonable price” clause was struck, he said, there was a threefold increase in partnership deals.

The N.I.H. can collect royalties from successful products to help offset the costs of the research, but so far these royalties have been small, amounting to an estimated $135 million in the last fiscal year from 870 licenses, with the bulk of the money coming from a small number of drugs.

“We’re not preoccupied with financial value,” Dr. Rohrbaugh said. “Our mission is treatment of people and improving public health.”

In that regard, the government’s bet on a small company like Kite, which might have seemed risky, appears to be paying off so far.

Dr. Belldegrun has largely delivered on promises to raise money, assemble an experienced staff, build the factory, conduct clinical trials and begin to apply for regulatory approval. Once considered the underdog to Novartis and Juno, Kite might be the first reach the market.

Photo

Scans of Mr. Karlson’s body before and after his treatment. In the cross-sections on the left, the arrows point to signs of lymphoma in areas such as his armpits, chest, spleen and pelvis. Credit National Cancer Institute

Academic centers and companies often drive harder bargains in licensing technology. In some cases, academic centers own a stake in a company they license technology to, allowing them to reap a financial windfall if the company does well. Both the Hutchinson cancer center and Sloan Kettering have owned stock in Juno and are entitled to substantial payments — up to $350 million and $150 million — if Juno's stock reaches certain levels.

The N.I.H. does not take equity positions in companies to avoid an appearance of a conflict of interest. So to critics of the government deals, drug prices are crucial to understanding taxpayer value. After all, they ask, is a drug truly widely available — which is what the government says is its measure of success — if it costs too much for some people?

Rachel Sachs, an associate law professor at Washington University in St. Louis and expert in innovation policy, said the government had every right to seek price concessions. She noted that the government, through Medicare and Medicaid, was effectively buying its inventions back from itself. "The public is paying for the research and to the extent that many people, if not most, will pay through public insurance, we're paying again," she said.

Hillary Clinton, in her campaign for president, promised to set new rules for federal support of research so that Americans "get the value they deserve" for the money taxpayers spend in supporting research. It is not clear how President-elect Donald J. Trump will approach these issues; he has said he favors reducing health care costs, but Republicans, who control Congress, too, have opposed government involvement in price setting.

One mechanism to control pricing already exists. It is called march-in rights, and it lets the N.I.H. take back control of a patent on an invention made with federal funding if the drug is not being made available to the public on reasonable terms. The tool has gone unused.

Earlier this year, Knowledge Ecology International and another advocacy group, the Union for Affordable Cancer Treatment, petitioned the agency to exercise march-in rights on Xtandi, a prostate cancer drug that was developed by federally funded researchers at U.C.L.A. It said the price in the United States of about $129,000 a year, two to four times that in other developed countries, meant the drug was not reasonably available. The effort was supported by other public interest groups and some Democratic members of Congress.

U.C.L.A. made more than $500 million by selling its royalty rights to the drug. But the N.I.H. declined to exercise its march-in rights on Xtandi, arguing that it was not qualified to judge whether a drug's price is reasonable and that a high price does not mean a drug is not being made available to the public.

"N.I.H. has made it clear that its job is not to decide prices of drugs, period," Dr. Rohrbaugh said

Kite says it has not decided what to charge for KTE-C19, but Dr. Belldegrun hinted that Kite's therapy might be relatively expensive because ideally it would be a single treatment that would cure the patient, not a drug that would have to be taken continuously. He added that Kite would take steps to make sure that everyone who needed the drug could get it.

Meantime, the relationship between Kite and the National Cancer Institute is expanding to develop treatments for other cancers, including one technique Dr. Rosenberg thinks could be used to attack solid tumors like colon, breast and lung cancer.

“The potential for broad applicability is huge,” he said.

That could mean many lives saved and maybe more billion-dollar drugs for Kite and its investors, with the American taxpayer right in the middle of the deal.

Like the Science Times page on Facebook. | Sign up for the Science Times newsletter.

--

Joseph P. Allen
President
Allen and Associates
60704 Rt. 26, South
Bethesda, OH 43719
(W) 740-484-1814
(c) b6
www.allen-assoc.com

--

Joseph P. Allen
President
Allen and Associates
60704 Rt. 26, South
Bethesda, OH 43719
(W) 740-484-1814
(c) b6
www.allen-assoc.com

From: Freel, Rose (NIH/NCI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=E8AE9AAB7E3249E881BB573E9A189036-FREELRM]
Sent: 7/19/2018 12:04:38 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
CC: Rodriguez, Richard (NIH/NCI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8092cb5394e04733ac0d4d84d25f65e5-rodrigr]; Berkley, Dale (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5ee461c29f5045a49f0adf82caaa2f31-berkleyd]
Subject: RE: Prospective Grant of an Exclusive Patent License: Development of an Anti-Mesothelin Chimeric Antigen Receptor (CAR) for the Treatment of Human Cancer to Atara Biotherapeutics Inc.
Attachments: Atara-Biotherapeutics-NIH-13Jul2018-corrected.pdf

Hi Mark,

Just following up on this, let me know your thoughts on a response to KEI.

Thanks!
Rose

--
Rose Santangelo Freel, Ph.D.
Senior Technology Transfer Manager
National Cancer Institute
P 301-624-1257 | rose.freel@nih.gov

From: Freel, Rose (NIH/NCI) [E]
Sent: Tuesday, July 17, 2018 8:11 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Cc: Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>; Berkley, Dale (NIH/OD) [E] <BerkleyD@OD.NIH.GOV>
Subject: FW: Prospective Grant of an Exclusive Patent License: Development of an Anti-Mesothelin Chimeric Antigen Receptor (CAR) for the Treatment of Human Cancer to Atara Biotherapeutics Inc.

Hi Mark,

Attached are comments I received from KEI on the FR Notice for the Prospective Grant to Atara. Can you please tell me if and how we should respond?

Thanks!
Rose

--
Rose Santangelo Freel, Ph.D.
Senior Technology Transfer Manager
National Cancer Institute
P 301-624-1257 | rose.freel@nih.gov

From: James Love <james.love@keionline.org>
Sent: Friday, July 13, 2018 4:45 PM
To: Freel, Rose (NIH/NCI) [E] <rose.freel@nih.gov>
Cc: Tim Reed <Tim@haiweb.org>; Luis Gil Abinader <luis.gil.abinader@keionline.org>; Merith Basey <merith@essentialmedicine.org>; Alex Lawson <alawson@socialsecurityworks.org>; Fran Quigley

b6; Baker, Brook <b.baker@northeastern.edu>; Meg Jones-Monteiro <mjonesmonteiro@iccr.org>; Manon Ress <MANON.RESS@cancerunion.org>; Claire Cassedy <claire.cassedy@keionline.org>; Thiru Balasubramaniam <thiru@keionline.org>
Subject: Re: Prospective Grant of an Exclusive Patent License: Development of an Anti-Mesothelin Chimeric Antigen Receptor (CAR) for the Treatment of Human Cancer to Atara Biotherapeutics Inc.

Dear Dr. Freel,

I'm attaching a corrected copy of the comments. The difference was just the spelling of CFR, which had been transposed in the earlier version.

Jamie

On Fri, Jul 13, 2018 at 4:09 PM, James Love <james.love@keionline.org> wrote:

> Dr. Freel,
>
> Attached are comments on the Atara license from:
>
> Health Action International (HAI)
> Health GAP
> Interfaith Center on Corporate Responsibility (ICCR)
> Knowledge Ecology International (KEI)
> People of Faith for Access to Medicines (PFAM)
> Social Security Works (SSW)
> Union for Affordable Cancer Treatment (UACT)
> Universities Allied for Essential Medicines (UAEM)
>
> --
> James Love. Knowledge Ecology International
> http://www.keionline.org/donate.html
> KEI DC tel: +1.202.332.2670, US Mobile: +1.202.361.3040, Geneva Mobile: +41.76.413.6584, twitter.com/jamie_love

--
James Love. Knowledge Ecology International
http://www.keionline.org/donate.html
KEI DC tel: +1.202.332.2670, US Mobile: +1.202.361.3040, Geneva Mobile: +41.76.413.6584, twitter.com/jamie_love

July 13, 2018

Rose M. Freel, Ph.D.
Licensing and Patenting Manager
NCI Technology Transfer Center
Email: *rose.freel@nih.gov*.

Re: Prospective Grant of an Exclusive Patent License: Development of an Anti-Mesothelin Chimeric Antigen Receptor (CAR) for the Treatment of Human Cancer to Atara Biotherapeutics Inc.

Dear Dr. Rose M. Freel:

We are writing to provide comments on the prospective grant of an exclusive patent license for the development of an anti-mesothelin Chimeric Antigen Receptor (CAR) for the treatment of human cancer to Atara Biotherapeutics Inc., as noticed in the Federal Register: 83 FR 30448.

According to the notice in the *Federal Register,* "the prospective exclusive license territory may be worldwide," and the field of use is described as:

> "The development of a mesothelin chimeric antigen receptor (CAR)-based immunotherapy using autologous or allogeneic T cells either transduced with a retroviral vector (including lentiviral vectors) or modified using a gene-editing technology, wherein the vector expresses a CAR comprising:
>
> (1) Single antigen specificity for binding to mesothelin, and
>
> (2) at least (a) the complementary determining region (CDR) sequences of the anti-mesothelin antibody known as m912, and (b) a T cell signaling domain; for the prophylaxis and treatment of mesothelin-expressing human cancers.'"

The NIH has been asked but declined to extend the comment period so that the public would have had additional time to obtain information from the NIH or third parties on the budgets of clinical trials for either CAR T-cell trials, or trials involving anti-mesothelin therapies, or both. Related to this, the NIH has been asked for information regarding the budgets of 14 CAR T trials funded by the NIH, and that information is unfortunately not yet available.

Information about the costs of conducting CAR T trials is important in evaluating the proposal by the NIH to grant an exclusive license and the scope of rights included in any exclusive license (as is required by 35 USC § 209), including the years of exclusivity and the safeguards to ensure that the patented products, services or procedures are available to the public on reasonable terms (as is required by 35 USC § 201(f)). We suggest the NIH take measures to increase the transparency of the costs of R&D that the NIH funds. Our comments for this license contain suggestions that would increase transparency going forward, not only for R&D funded directly by the NIH, but also for R&D associated with the development of patented inventions owned by the NIH and licensed to third parties.

In the absence of public evidence that the NIH has estimated the costs of bringing this technology to market and evaluated the scope of rights necessary to induce such investment, we cannot support an exclusive license at this time.

If the NIH does in fact proceed with an exclusive license, these are provisions that we recommend be included in the terms of the license.

1. No discrimination against US residents in pricing

Prices in the U.S. for any drug, vaccine, medical device or other health technology using the invention should not be higher than the median price charged in the seven countries with the largest gross domestic product (GDP), that also have a per capita income of at least 50 percent of the United States, as measured by the World Bank Atlas Method.

2. Reduce term of exclusivity when revenues are large

The exclusivity of the license in the U.S. should be reduced by one year for every $500 million in revenue equivalents, earned after the first $1 billion, where revenue equivalent is defined as global cumulative sales plus market entry rewards as well as government grants or tax credits, for the product or products using the invention. The NIH could consider different benchmarks, based upon evaluating evidence of the costs of additional development of CAR T therapies, but the $1 billion and $.5 billion figures are at least a start to acknowledge that at some point, the returns on a government-funded invention are excessive, given the licensee's risk-adjusted investments.

3. Developing countries

The license should not be exclusive for countries with a per capita income that is less than 30 percent of the U.S.A. If the NIH does in fact provide exclusive rights in developing countries, the license holder should have an obligation to provide the NIH with a reasonable plan to make the drugs affordable and accessible in those countries, a condition the Gates Foundation has used for some patent licenses. In addition, if the licenses are exclusive in developing countries, the NIH should retain an explicit option to provide an additional license to the Medicines Patent Pool, if access is deemed insufficient in countries with incomes significantly lower than the United States.

5. Transparency

The licensee should be required to file an annual report to the NIH, available to the public, on the research and development (R&D) costs associated with the development of any product that uses the invention, including reporting separately the outlays on each clinical trial. We will note that this is not a request to see a company business plan or license application. We are asking that going forward the company be required to report on actual R&D outlays to develop the subject inventions. We recognize that 35 USC § 209(f) requires applicants to provide a development plan and that such a plan is not subject to FOIA, and that the regulations regarding reports relating to the development plan are also limited as to the scope of and access to the reports, under 37 CFR 404.14 - Confidentiality of information, and that reports required under 37 CFR 404.5(b)(6) are considered confidential information. However, the NIH can ask for other reports, which can be made public. For example, the NIH required reports from the Icahn School of Medicine at Mount Sinai on access to Fabrazyme, and those reports were eventually made public under FOIA. The federal government needs to revise the regulations regarding the confidentiality of reporting of federally funded inventions, but even now, as the Fabrazyme case illustrates, there may be some flexibility, particularly in this case, where the reports are not specifically related to the company's development plan, and such transparency is clearly in the public interest.

Sincerely,

Health Action International (HAI)
Health GAP
Interfaith Center on Corporate Responsibility (ICCR)
Knowledge Ecology International (KEI)
People of Faith for Access to Medicines (PFAM)
Social Security Works (SSW)
Union for Affordable Cancer Treatment (UACT)
Universities Allied for Essential Medicines (UAEM)

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

b5

From: Hammersla, Ann (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=87FB28AA23744C0B855EF0683AC2E8B4-HAMMERSLAA]
Sent: 8/29/2018 5:16:45 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: FW: Rydapt
Attachments: RE: U.S. Patents U.S. 8,222,244, and U.S. 7,973,031; Rydapt; RE: James Douglas Griffin; CA066996; RE: Rydapt and Steven Coutre; RE: DK050654 (1997-2002) - James Douglas Griffin/Dana Farber; Funding Summary 08292018ah.docx

Mark:

As a follow-up to my previous questions re this technology and your response I have attached several documents from NIH's Program Officer's review as well as the response from DFCI. b5 b5 and before talking with Dale, a review by you would be helpful. See my funding summary attached.

Let me know when you are available to discuss.

Ann

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Friday, August 17, 2018 11:11 AM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Subject: RE: Rydapt

Ann:

b5

From: Hammersla, Ann (NIH/OD) [E]
Sent: Wednesday, August 15, 2018 1:52 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: Rydapt

Hello Mark:

b5

Can you review?

Ann

--
Ann M. Hammersla, J.D.
Director
Division of Extramural Inventions and Technology Resources
Office of Policy for Extramural Research Administration
Rockledge 1, Suite 310
6705 Rockledge Drive
Bethesda, Maryland 20892-7974
PHONE: 301-435-0745

From: Sclar, Gary M. [Gary_Sclar@DFCI.HARVARD.EDU]
Sent: 4/25/2018 6:59:36 PM
To: Hammersla, Ann (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=87fb28aa23744c0b855ef0683ac2e8b4-hammerslaa]
CC: Rice Ackman, Rachel E. [Rachel_RiceAckman@DFCI.HARVARD.EDU]; Libka, Hilary [Hilary_Libka@DFCI.HARVARD.EDU]
Subject: RE: U.S. Patents U.S. 8,222,244, and U.S. 7,973,031; Rydapt
Attachments: DFCI Response Re US Patent Nos. 8,222,244 and 7,973,031.pdf

Dear Ms. Hammersla,

Attached please find the details of our evaluation of the above-referenced patents and NIH Grants P01 CA066996 and RC1 CA147386, as you requested.

As a result of our evaluation, DFCI appropriately did not report that federal funding was used in the conception or reduction to practice of the subject matter of the patents. We are happy to set up a call to discuss further, if this would be useful to you.

Regards,

Gary

Gary M. Sclar, J.D.
Vice President, Dana-Farber Innovations
Dana-Farber Cancer Institute
Belfer Office for Dana-Farber Innovation
450 Brookline Ave., Boston, MA 02215
Phone: 617-632-5807 ▪ Fax: 617-632-4012
Email: gary_sclar@dfci.harvard.edu

From: Sclar, Gary M.
Sent: Thursday, April 12, 2018 1:59 PM
To: 'Hammersla, Ann (NIH/OD) [E]' <hammerslaa@mail.nih.gov>
Cc: Rice Ackman, Rachel E. <Rachel_RiceAckman@DFCI.HARVARD.EDU>; Libka, Hilary <Hilary_Libka@DFCI.HARVARD.EDU>
Subject: RE: U.S. Patents U.S. 8,222,244, and U.S. 7,973,031; Rydapt

Dear Ms. Hammersla,

Thank you for your email. DFCI is aware of KEI's concerns related to grants P01 CA066996 and RC1 CA147386. We have been reviewing this matter internally and plan to provide you with the results of that evaluation by April 25, 2018, as requested.

Regards,

Gary

Gary M. Sclar, J.D.
Vice President, Dana-Farber Innovations
Dana-Farber Cancer Institute
Belfer Office for Dana-Farber Innovation

450 Brookline Ave., Boston, MA 02215
Phone: 617-632-5807 ▪ Fax: 617-632-4012
Email: gary_sclar@dfci.harvard.edu

From: Hammersla, Ann (NIH/OD) [E] [mailto:hammerslaa@mail.nih.gov]
Sent: Thursday, April 12, 2018 8:33 AM
To: Sclar, Gary M. <Gary_Sclar@DFCI.HARVARD.EDU>
Subject: U.S. Patents U.S. 8,222,244, and U.S. 7,973,031; Rydapt

Dear Mr. Sclar:

On March 21, 2018 Knowledge Ecology International (KEI) brought to the National Institutes (NIH) attention its findings that NIH funding to the Dana-Farber Cancer Institute (Dana-Farber) for Dr. James Griffin was used in the development of the inventions that led to two United States patents referenced above. These patents identify Dr. Griffin as an inventor and were issued jointly to Dana-Farber and Novartis AG. The Food and Drug Administration's Orange Book identifies these patents as being used in the manufacture of Rydapt® (INN midostaurin).

Two NIH grants, P01 CA066996 and RC1 CA147386, have been identified as sources of research funding that may have led to the conception or the reduction to practice of the subject inventions that led to these two patents. Dana Farber disclosed to NIH 18 subject inventions in iEdison with Dr. Griffin as an inventor but has not reported the issuance of these two identified patents.

KEI, in its attached March 21, 2018 letter requests that NIH take title to these two identified patents in accordance with 37 C.F.R. § 401.14(a)(d), require U.S. Manufacturing as required by 37 C.F.R. § 401.14(a)(i), and/or or based on NIH's findings of Dana-Farber's lack of compliance in disclosing or acknowledging NIH support of the two patents in question use NIH's rights as set forth at 37 C.F.R. § 401.14(a)(j).

As part of the NIH's Bayh-Dole Act oversight responsibilities, NIH requests that within ten business days of the date of this email, Dana-Farber provide detailed information concerning NIH's research funding to Dana-Farber for research by Dr. Griffin, including the two NIH grants cited above, and its evaluation of whether federal funding was used in the conception or reduction to practice of the inventions that led to the granting of these two patents.

If you have any questions, you can contact me at the number and email address below.

Ann Hammersla

--

Ann M. Hammersla, J.D.
Director
Division of Extramural Inventions and Technology Resources
Office of Policy for Extramural Research Administration
Rockledge 1, Suite 310
6705 Rockledge Drive
Bethesda, Maryland 20892-7974
PHONE: 301-435-0745

The information in this e-mail is intended only for the person to whom it is addressed. If you believe this e-mail was sent to you in error and the e-mail contains patient information, please contact the Partners Compliance HelpLine at http://www.partners.org/complianceline . If the e-mail was sent to you in error but does not contain patient information, please contact the sender and properly dispose of the e-mail.

DANA-FARBER
CANCER INSTITUTE

Dana-Farber Cancer Institute
450 Brookline Avenue
Boston, Massachusetts 02215-5450
www.dana-farber.org

April 25, 2018

SUBJECT: U.S. Patent Nos. 8,222,244 and 7,973,031; Rydapt® midostaurin

Dear Ms. Hammersla:

On April 12, 2018, you requested that DFCI share its evaluation of whether federal funding was used in the conception or reduction to practice of the subject matter claimed in the patents referenced in the subject line of this email. As described in more detail below, federal funding (specifically, P01 CA066996 and RC1 CA147386) was not used to support this scientific work. As a result, DFCI appropriately did not report that federal funding was used in the conception or reduction to practice of the subject matter.

b4

b4

b4

Summary

Based on the above findings regarding the patents, the grants, and the *Cancer Cell* paper, DFCI submits that federal funding was not used to support the conception or reduction to practice of the subject matter claimed in U.S. Patent Nos. 8,222,244 and 7,973,031. As a result, it was appropriate for DFCI to not report this invention to iEdison.

Please do not hesitate to reach out again if we can be of any additional assistance.

Sincerely,

b6

Gary Sclar

cc:

Dr. James Griffin
Hilary Libka
Kelly Maxwell
Rachel Rice Ackman

From: Merritt, William (NIH/NCI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=33AED7EEF02943408617245830EB07A8-MERRITTW]
Sent: 7/11/2018 3:50:27 PM
To: Hammersla, Ann (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=87fb28aa23744c0b855ef0683ac2e8b4-hammerslaa]
Subject: RE: James Douglas Griffin; CA066996

Ann - I checked the P01 again,

Project 1 in CA066996-06 was led by Dr. Griffin. Title: Tyrosine Kinase Oncogenes in AML Aims:

Specific Aim 1. Determine the mechanisms of activation of FLT3 by mutations in AML.
A) Internal tandem duplications of the juxta-membrane domain of FLT3
B) Point mutations of FLT3 in the kinase domain

Specific Aim 2. Determine the contribution of FLT3 to transformation of AML cells and identify the signaling pathways involved.

Specific Aim 3. Preclinical translational studies with FLT3
A) Examine the effects of small molecule FLT3 inhibitors on dimerization, kinase activity, and signaling.
B) Determine if combinations of signal transduction inhibitors are synergistic in preclinical models of AML
C) Determine if FLT3 inhibitors can be combined with immunotherapy
D) Generate monoclonal antibodies that recognize mutant FLT3 receptors
E) Develop screens for other activated tyrosine kinases in AML.

Project 2 was led by the PI of the whole program project, Dr. Gilliland. Title, Murine models of FLT3-mediated myeloid leukemias

Specific Aim 1. Characterize the transforming properties of FLT3-ITD in vivo in a murine bone marrow transplant assay, and determine the therapeutic efficacy of the FLT3 inhibitor CT535-18.
Specific Aim 2. Characterize cooperativity of FLT3-ITD in transgenic cathepsin G-PML/RARcr transgenic mice.
Specific Aim 3. Characterize FLT3-ITD cooperativity in AMLI/ETO conditional knock-in mice.
Specific Aim 4. Characterize FLT3-ITD cooperation with C/EBPo loss of function mutations in CYEBPu conditional knock-out mice.
Specific Aim 5. Construct and characterize PLT3-ITD conditional knock-in mice.

b5

Bill

Wiliam D. Merritt, Ph.D.
Program Director

Clinical Investigations Branch
Cancer Therapy Evaluation Program
Division of Cancer Treatment and Diagnosis
National Cancer Institute
Ph: 240-276-6137

From: Hammersla, Ann (NIH/OD) [E]
Sent: Wednesday, July 11, 2018 10:59 AM
To: Merritt, William (NIH/NCI) [E] <merrittw@mail.nih.gov>
Cc: Mooney, Margaret (NIH/NCI) [E] <mooneym@ctep.nci.nih.gov>
Subject: FW: James Douglas Griffin; CA066996

Good Morning Bill:

I have a follow-up question for you:

b5

Thank you again for your assistance.

Ann

From: Hammersla, Ann (NIH/OD) [E]
Sent: Monday, July 09, 2018 6:08 AM
To: Merritt, William (NIH/NCI) [E] <merrittw@mail.nih.gov>
Cc: Mooney, Margaret (NIH/NCI) [E] <mooneym@ctep.nci.nih.gov>
Subject: RE: James Douglas Griffin; CA066996

Good Morning Bill:

Thank you for your detailed analysis. I will keep you updated on the next steps.

Ann

From: Merritt, William (NIH/NCI) [E]
Sent: Friday, July 06, 2018 7:58 PM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Cc: Mooney, Margaret (NIH/NCI) [E] <mooneym@ctep.nci.nih.gov>
Subject: RE: James Douglas Griffin; CA066996

Ann –

I'm very sorry for the delay in responding, but finally now today I have had a (first) chance to get to this and other long delayed work, since some regular meetings were canceled.

b5

Regards,
Bill Merritt

Wiliam D. Merritt, Ph.D.
Program Director
Clinical Investigations Branch
Cancer Therapy Evaluation Program
Division of Cancer Treatment and Diagnosis
National Cancer Institute
Ph: 240-276-6137

From: Hammersla, Ann (NIH/OD) [E]
Sent: Monday, June 25, 2018 10:57 AM
To: Merritt, William (NIH/NCI) [E] <merrittw@mail.nih.gov>
Subject: FW: James Douglas Griffin; CA066996

Good Bill:

Do you have any questions regarding your review of CA066996?

Ann

From: Merritt, William (NIH/NCI) [E]
Sent: Monday, May 21, 2018 3:06 PM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Subject: RE: James Douglas Griffin; CA066996

Ann,

Thanks for this b5

Will be in touch,
Bill

Wiliam D. Merritt, Ph.D.
Program Director
Clinical Investigations Branch
Cancer Therapy Evaluation Program
Division of Cancer Treatment and Diagnosis

National Cancer Institute
Ph: 240-276-6137

From: Hammersla, Ann (NIH/OD) [E]
Sent: Monday, May 21, 2018 2:36 PM
To: Merritt, William (NIH/NCI) [E] <merrittw@mail.nih.gov>
Subject: FW: James Douglas Griffin; CA066996

Dear Bill:

Thank you for taking your time today to discuss CA066996 and if the supported research was used for the conception or reduction of Rydapt.

b5

Ann

From: Hammersla, Ann (NIH/OD) [E]
Sent: Tuesday, May 15, 2018 3:23 PM
To: Merritt, William (NIH/NCI) [E] <merrittw@mail.nih.gov>
Subject: RE: James Douglas Griffin; CA066996

Dear Bill:

I have attached the KEI request for NIH to take title or other actions to the patents in question. I have also attached Dana Farber's response and 3 citations to publications (2 have abstracts) that link Dr. Griffin's funding on two publications to CA066996. I have also identified over 100 other publications that are being reviewed.

I will send you an outlook meeting time for Monday. Thank you again for your assistance.

Ann

From: Merritt, William (NIH/NCI) [E]
Sent: Tuesday, May 15, 2018 11:33 AM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Subject: RE: James Douglas Griffin; CA066996

Ann,

I am leaving town very soon to attend a conference the rest of the week. So next Monday morning would be the first opportunity to talk. It may be helpful to send the information as background to me so I can look it over before we speak.

Best regards,
Bill Merritt

From: Hammersla, Ann (NIH/OD) [E]
Sent: Tuesday, May 15, 2018 11:17 AM
To: Merritt, William (NIH/NCI) [E] <merrittw@mail.nih.gov>
Subject: James Douglas Griffin; CA066996

Dear Dr. Merritt:

NIH received a request from Knowledge Ecology International (KEI) requesting NIH to take multiple actions, including, taking title to certain patents filed by the Dana Farber Institute for inventions made by Dr. James Douglas Griffin that have led to the therapeutic Rydapt®. According to QVR you are listed as the PO for the above grant that Dr. Griffin is supported on. b5 b5 Rydapt® is used for the treatment of acute myleloid leukemia, myelodysplastic syndrome and advanced systemic mastocytosis. There are 2 patents that Dr. Griffin is identified as an inventor that the FDA reports are used in the commercialization of Rydapt®. Both of the patents' abstracts state:

> The present invention relates to the use of staurosporines derivatives for the preparation of a drug for the treatment of diseases involving deregulated FLT3 receptor tyrosine kinase activity, especially for the curative and/or prophylactic treatment of leukemias and myelodysplastic syndromes, and to a method of treating diseases involving deregulated FLT3 receptor tyrosine kinase activity.

Before sending you additional background information you may need to identify the issues that have been raised, it may be helpful if we talked first. Or, if you prefer I can forward you the information received by KEI and the summaries prepared thus far for your review.

Please let me know when you are available for a 30 minute discussion. If it helps I am available this Thursday or Friday afternoon and Monday May 21 in the morning. Let me know if you would like to receive the background information before we talk.

Thank you in advance for your assistance.

Ann

--

Ann M. Hammersla, J.D.
Director
Division of Extramural Inventions and Technology Resources
Office of Policy for Extramural Research Administration
Rockledge 1, Suite 310
6705 Rockledge Drive
Bethesda, Maryland 20892-7974
PHONE: 301-435-0745

From: Hammersla, Ann (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=87FB28AA23744C0B855EF0683AC2E8B4-HAMMERSLAA]
Sent: 8/28/2018 6:25:22 PM
To: Karin Immergluck [Karin.Immergluck@stanford.edu]
Subject: RE: Rydapt and Steven Coutre

Dear Karin:

Thank you for Stanford's review.

Ann

From: Karin Immergluck <Karin.Immergluck@stanford.edu>
Sent: Thursday, August 16, 2018 6:41 PM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Subject: Re: Rydapt and Steven Coutre

Dear Ann,

I can confirm that the only two NIH grants that were awarded to Dr. Coutre during the relevant period prior to the filing of the below-mentioned Novartis-owned U.S. utility patent have no subject matter overlap with that patent. Furthermore, Dr. Coutre had been involved in Novartis-sponsored clinical trials just prior to the filing of the below-mentioned Novartis-owned patent.

Kind regards,
Karin

From: "Hammersla, Ann (NIH/OD) [E]" <hammerslaa@mail.nih.gov>
Date: Thursday, August 16, 2018 at 5:32 AM
To: Karin Immergluck <Karin.Immergluck@stanford.edu>
Subject: RE: Rydapt and Steven Coutre

Dear Karin:

From 1192-2008 Dr. Coutre had support from NIH's Research Resources Institute on grants M01 – RR000070

2014 – 2018 Dr. Coutre has been funded with NIH grants U10 CA180816

Ann

From: Karin Immergluck <Karin.Immergluck@stanford.edu>
Sent: Wednesday, August 15, 2018 5:03 PM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Subject: Re: Rydapt and Steven Coutre

Ann,

Just a quick follow up: Since you noticed that Dr. Coutre had NIH grants around the time of the patent filing in 2004, did you make a note of which NIH institutes were funding him? It's apparently not a straight-forward database exercise to dig up records for the early 2000s. If you don't have the information, we'll try going through his department manager's records.

Thanks,
Karin

From: "Hammersla, Ann (NIH/OD) [E]" <hammerslaa@mail.nih.gov>
Date: Wednesday, August 15, 2018 at 9:36 AM
To: Karin Immergluck <Karin.Immergluck@stanford.edu>
Subject: FW: Rydapt and Steven Coutre

Hello Karin:

I am following-up on my email below regarding Dr. Steven Coutre and the commercialization of Rydapt®. NIH is finishing its review and its important to know from Stanford whether, in its opinion, NIH funding that was granted to Dr. Coutre contributed to or was the conception or reduction to practice of a subject invention for Rydapt®.

Ann

From: Hammersla, Ann (NIH/OD) [E]
Sent: Wednesday, July 11, 2018 11:25 AM
To: 'karin.immergluck@stanford.edu' <karin.immergluck@stanford.edu>
Subject: Rydapt and Steven Coutre

Dear Karin:

Before Kathy retired I mentioned to her that one of Stanford's researchers, Steven Coutre, may have been a named inventor on one of Norvatis' patents that has been identified by the FDA as being used in the commercialization of Rydapt®. U.S. Patent 8,575,146 filed June 17, 2004 and issued November 5, 2013 identifies Steven Coutre from Stanford, California and Novartis is the assignee.

These circumstances came to my attention due to a request from Knowledge Express International (KEI) for NIH to use its rights, including march-in, on the drug Rydapt®. I have attached KEI's public request. In reviewing NIH's research support in the development of Rydapt® and included in KEI's request is the identification of this patent. In reviewing NIH's iEdison records, no disclosures were made to NIH by Stanford for Dr. Coutre. Dr. Coutre has had NIH funding during the same time frame as these patents were filed.

Could you please confirm whether Dr. Coutre is the inventor on this patent and that no NIH-funding granted to Dr. Coutre contributed to or was the basis of a subject invention of Rydapt® while working on NIH-funding.

Thank you for your assistance.

Ann Hammersla

--
Ann M. Hammersla, J.D.
Director
Division of Extramural Inventions and Technology Resources
Office of Policy for Extramural Research Administration

Rockledge 1, Suite 310
6705 Rockledge Drive
Bethesda, Maryland 20892-7974
PHONE: 301-435-0745

From: Hammersla, Ann (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=87FB28AA23744C0B855EF0683AC2E8B4-HAMMERSLAA]
Sent: 8/15/2018 6:20:22 PM
To: Bishop, Terry (NIH/NIDDK) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=bff001cf0f824d4196e8c564e5f50bac-bishopt]
Subject: RE: DK050654 (1997-2002) - James Douglas Griffin/Dana Farber

Dear Terry: Thank you again for your assistance. Ann

From: Bishop, Terry (NIH/NIDDK) [E]
Sent: Wednesday, August 15, 2018 2:20 PM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Subject: RE: DK050654 (1997-2002) - James Douglas Griffin/Dana Farber

Hello, Ann,

As promised, here is the abstract from Project 2 (led by Dr. James Griffin) of the Program Project, 2 P01 DK050654-06 (Alan D. D'Andrea, PI) in Fiscal Year 2002.

NOTE: This is the oldest grant application I can find in the electronic database. There are no applications available for years preceding 2002, although NIDDK did fund this Program Project beginning in 1997.

I searched the entire P01 application for "FLT3" and "PKC412" and did not find any matches.

So, here is the abstract of Dr. Griffin's project as stated in 2002:

Chronic myeloid leukemias are caused by activated tyrosine kinase oncogenes, most often by BCR/ABL, or the related oncogenes TEL/ABL, TEL/JAK2, or TEL/PDGFR. The goal of this project is to understand in detail the signal transduction pathways activated by BCR/ABL and related oncogenes that are relevant for transformation of hematopoietic cells. Using BCR/ABL as the best-studied example, this kinase is believed to function by phosphorylating itself and adjacent cell proteins, and by phosphorylating other proteins that are brought in by adapter molecules. This results in activation of a variety of signaling pathways that ultimately block apoptosis, deregulate cell cycle control, alter adhesion and homing, and cause genetic instability. A particular focus of this project period will be phosphotidylinositol signaling, which we and others have shown is required for transformation, probably because of prominent effects on apoptosis and cell cycle deregulation. We would like to understand how PI3K is activated and determine the downstream targets particularly those related to viability signaling. Also, in preliminary studies we have shown that SHIP, an inositol 5-phophatase, is downregulated by BCR/ABL. SHIP activity would be expected to modulate the lipids that accumulated downstream of PI3K. This is of interest since a SHIP knock out mouse develops a myeloproliferative syndrome, suggesting that there may be certain PI3K products that are more important for hematopoiesis than others. Finally, efforts will be focused on understanding the differences in signaling by the 3 known forms of BCR/ABL, encoding pi90, p210, or p230; and understanding the differences between BCR/ABL and v-ABL. In particular, pathways initiated because of phosphorylation of Y177 of BCR seem to be of particular interest, as this single tyrosine residue is needed to generate a myeloproliferative disorder in mice. Overall, identification of critical signaling intermediates will be useful for many reasons, but particularly to identify potential targets for drug development, especially for drugs that would be synergistic with ST1571.

b5

Thanks,

--Terry

Terry Rogers Bishop, Ph.D.
Hematology Program Director
Division of Kidney, Urologic,
and Hematologic Diseases (KUH)

Cell: b6

National Institute of
Diabetes and Digestive
and Kidney Diseases

NIH . . . Turning Discovery Into Health®

From: Hammersla, Ann (NIH/OD) [E]
Sent: Wednesday, August 15, 2018 10:48 AM
To: Bishop, Terry (NIH/NIDDK) [E] <BishopT@EXTRA.NIDDK.NIH.GOV>
Subject: FW: DK050654 (1997-2002) - James Douglas Griffin/Dana Farber

Good Morning:

I am following-up on the review of the above referenced grant. Would you like to discuss?

Ann

From: Bishop, Terry (NIH/NIDDK) [E]
Sent: Thursday, May 24, 2018 9:07 AM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Subject: Re: DK050654 (1997-2002) - James Douglas Griffin/Dana Farber

Good morning, Ann.

Thank you for the "heads up" on this complicated issue.

Would you be available for a phone call today at 10:30am?

--Terry

Terry Rogers Bishop, PhD
Hematology Program Director
NIH/NIDDK/DKUHD
Cell: b6

On May 24, 2018, at 8:35 AM, Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov> wrote:

> Good Morning Terry:
>
> NIH received a request from Knowledge Ecology International (KEI) requesting NIH to take multiple actions, including, taking title to certain patents filed by the Dana Farber Institute for inventions made by Dr. James Douglas Griffin. These inventions and the resulting patents FDA approved to be used in

the commercialization of the therapeutic Rydapt®. It is Dana Farber's position that no NIH support was used in the conception or reduction to practice of the identified inventions and resulting patents.

b5

b5 Rydapt® is used for the treatment of acute myleloid leukemia, myelodysplastic syndrome and advanced systemic mastocytosis. There are 2 patents that Dr. Griffin is identified as an inventor and both of the patent abstracts state:

> The present invention relates to the use of staurosporines derivatives for the preparation of a drug for the treatment of diseases involving deregulated FLT3 receptor tyrosine kinase activity, especially for the curative and/or prophylactic treatment of leukemias and myelodysplastic syndromes, and to a method of treating diseases involving deregulated FLT3 receptor tyrosine kinase activity.

Before sending you additional background information you may need to identify the issues that have been raised, it may be helpful if we talked first. Or, if you prefer I can forward you the information received by KEI and the summaries prepared thus far for your review.

Please let me know when you are available for a 30-minute discussion. If it helps I am available this morning and Tuesday May 28th. Let me know if you would like to receive the background information before we talk.

Thank you in advance for your assistance.

Ann

From: Bishop, Terry (NIH/NIDDK) [E]
Sent: Thursday, May 24, 2018 8:05 AM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Cc: Pike, Robert (NIH/NIDDK) [E] <pikera@niddk.nih.gov>; Perry-Jones, Aretina (NIH/NIDDK) [E] <PerryA@extra.niddk.nih.gov>; Kenley, Charlette (NIH/NIDDK) [E] <KenleyC@EXTRA.NIDDK.NIH.GOV>
Subject: Re: DK050654 (1997-2002) - James Douglas Griffin/Dana Farber

Thank you, Ann.

--Terry

Terry Rogers Bishop, PhD
Hematology Program Director
NIH/NIDDK/DKUHD
Cell: b6

On May 24, 2018, at 7:49 AM, Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov> wrote:

> Thank you to all for your assistance.
> Dr. Bishop I will send you additional information.
>
> Ann
>
> ---
>
> **From:** Pike, Robert (NIH/NIDDK) [E]
> **Sent:** Wednesday, May 23, 2018 1:22 PM

To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Cc: Bishop, Terry (NIH/NIDDK) [E] <BishopT@EXTRA.NIDDK.NIH.GOV>; Perry-Jones, Aretina (NIH/NIDDK) [E] <PerryA@extra.niddk.nih.gov>; Kenley, Charlette (NIH/NIDDK) [E] <KenleyC@EXTRA.NIDDK.NIH.GOV>
Subject: FW: DK050654 (1997-2002) - James Douglas Griffin/Dana Farber

Hi Ann,

Dr. Terry Bishop (copied here) is the contact for the referenced grant.

Thanks,
Bob

Bob Pike
Chief Grants Management Officer
National Institute of Diabetes and Digestive and Kidney Diseases
National Institutes of Health
Bethesda, MD 20892
Phone: (301) 594-8854

From: Bishop, Terry (NIH/NIDDK) [E]
Sent: Wednesday, May 23, 2018 1:09 PM
To: Pike, Robert (NIH/NIDDK) [E] <pikera@niddk.nih.gov>; Perry-Jones, Aretina (NIH/NIDDK) [E] <perrya@extra.niddk.nih.gov>
Cc: Kenley, Charlette (NIH/NIDDK) [E] <kenleyc@extra.niddk.nih.gov>
Subject: RE: DK050654 (1997-2002) - James Douglas Griffin/Dana Farber

Yes, it is I.

--Terry

Terry Rogers Bishop, Ph.D.
Hematology Program Director
Division of Kidney, Urologic,
and Hematologic Diseases (KUH)

Cell: b6

<image002.jpg>

NIH . . . Turning Discovery Into Health®

From: Pike, Robert (NIH/NIDDK) [E]
Sent: Wednesday, May 23, 2018 8:50 AM
To: Perry-Jones, Aretina (NIH/NIDDK) [E] <perrya@extra.niddk.nih.gov>
Cc: Kenley, Charlette (NIH/NIDDK) [E] <kenleyc@extra.niddk.nih.gov>; Bishop, Terry (NIH/NIDDK) [E] <bishopt@extra.niddk.nih.gov>
Subject: FW: DK050654 (1997-2002) - James Douglas Griffin/Dana Farber

Aretina,

Can you please find out who the Program contact is for the referenced grant below and reply to Anna Hammersla in OER with a cc to me? IMPAC says it's Dr. Biship in 2006.

Thanks,
Bob

From: Hammersla, Ann (NIH/OD) [E]
Sent: Tuesday, May 22, 2018 2:21 PM
To: Pike, Robert (NIH/NIDDK) [E] <pikera@niddk.nih.gov>
Subject: DK050654 (1997-2002) - James Douglas Griffin/Dana Farber

Hello Dr. Pike:

NIH received a request from a 3rd party to take several steps, including taking ownership, of certain patents that may have been funded by NIH. David Badman was the PO on the above referenced grant and he is no longer at NIH. Can you recommend a PO that I can talk to about the NIDDK's support of research for Dr. Griffin?

The title of the above referenced grant for the first couple of years was "Abnormal Signal Transduction in Hematopoietic Disease" and "Signal Transduction in Hematopoietic Cells Mediated by Tyrosine Kinase Fusions."

Please let me know if you need additional information or if there is someone else I should talk to.

Thanks in advance for your help.

Ann

Ann M. Hammersla, J.D.
Director
Division of Extramural Inventions and Technology Resources
Office of Policy for Extramural Research Administration
Rockledge 1, Suite 310
6705 Rockledge Drive
Bethesda, Maryland 20892-7974
PHONE: 301-435-0745

b5

b5

From: Gadbois, Ellen (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0243D1D6E6F248268D2EDEC566C26C2A-GADBOISEL]
Sent: 7/20/2018 12:05:53 AM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: Re: CONFIDENTIAL list of attendees for Harvard meeting

I don't know anyone else on the list. Pretty small group.

Sent from my BlackBerry 10 smartphone.
Original Message
From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Thursday, July 19, 2018 17:38
To: Dodson, Sara (NIH/NIAID) [E]; Gadbois, Ellen (NIH/OD) [E]
Subject: CONFIDENTIAL list of attendees for Harvard meeting

I was invited to this closed meeting in Dec about " of government funding of drug development and the different strategies that are currently taken (and that have been proposed) to account for that contribution"
b6 has been active writing for years about use of march-in to reduce prices. b6 you probably know. We know b6 b6 are in the same camp. Of course we know b6 (odd that he would be coming). Do you know any of the others and their general positions on issues like this?

-----Original Message-----
From: Kesselheim, Aaron Seth,M.D.,M.P.H. <akesselheim@bwh.harvard.edu>
Sent: Thursday, July 19, 2018 5:30 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: Questions about CRADAs

We hope so. The (at this point, confidential) list of other invitees is below. We would welcome your participation as a member of the conversation throughout the meeting, or for a half-day period, or even as a guest speaker at lunch or dinner. We will operate under 'Chatham House Rules' such that there will be no quotes attributed to anyone.

Let me know what you think! We believe it will be very useful to have your perspective and contribution--

Best,
Aaron

b6

-----Original Message-----
From: Rohrbaugh, Mark (NIH/OD) [E] [mailto:rohrbaum@od.nih.gov]
Sent: Thursday, July 19, 2018 5:05 PM
To: Kesselheim, Aaron Seth,M.D.,M.P.H. <akesselheim@bwh.harvard.edu>
Subject: RE: Questions about CRADAs

External Email - Use Caution

Aaron:

I am considering your invitation to the Dec meeting. Will the attendees represent a breadth of thinking and opinions about this issue?

Thanks
Mark

-----Original Message-----
From: Kesselheim, Aaron Seth,M.D.,M.P.H. <akesselheim@bwh.harvard.edu>
Sent: Wednesday, July 18, 2018 4:05 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: Questions about CRADAs

So noted! This is all for our background knowledge. Thanks for responding!

Any initial thoughts about joining us in Boston for the December event?

ASK

-----Original Message-----
From: Rohrbaugh, Mark (NIH/OD) [E] [mailto:rohrbaum@od.nih.gov]
Sent: Wednesday, July 18, 2018 4:03 PM
To: Kesselheim, Aaron Seth,M.D.,M.P.H. <akesselheim@bwh.harvard.edu>
Subject: RE: Questions about CRADAs

External Email - Use Caution

Aaron:

Note that I do not give permission to publish or otherwise publicize my direct comments without permission.

By the late 1980s, NIH was using one standard model agreement for all types of CRADA collaborations. We noted later that some types of collaborations required fewer terms in this standard agreement. In particular, when the collaboration involved primarily the receipt and training in the use of unique research materials from a company, terms dealing with other matters such as human subjects, reports from the company, regular meetings between the parties, etc. were not relevant and therefore not needed. Rather than send a company lawyer a document with a number of nonrelevant terms to be deleted, NIH developed a M-CRADA stripped down to the terms relevant to or otherwise legally required in a collaboration involving primarily materials. It sped up negotiation and thus benefited both the NIH and the company providing the unique materials.

Since then other CRADA models were developed to suit particular types of commercial collaborations, e.g. clinical research.

CRADA partners do not decide on which model, NIH decides.

-----Original Message-----
From: Kesselheim, Aaron Seth,M.D.,M.P.H. <akesselheim@bwh.harvard.edu>
Sent: Wednesday, July 18, 2018 11:21 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: RE: Questions about CRADAs

Thanks Mark! This is very useful--I will read this over. Here are the questions we have, which may not be covered by this overview:

1. What's the difference between a CRADA and a Materials CRADA (MCRADA)? In particular, are there any cost benefits or differences in accessibility between a CRADA and an MCRADA?
2. Prior to 1996 (when the NIH initiated MCRADAs), could any of the signed CRADAs cover what is now included in an MCRADA?
3. How do potential CRADA partners decide between a CRADA and a MCRADA?
4. What motivated the NIH to introduce the MCRADA mechanism in 1996?

Let me know if this is worth a phone call.

On a different note, we're organizing a Radcliffe Seminar at Harvard this winter (December 11-12) on the subject of government funding of drug development and the different strategies that are currently taken (and that have been proposed) to account for that contribution. It's a small group session of like 15 or so experts in science, economics, law, and medicine from around the country. It would be great to have you join us if not for the whole time, at least as a guest/featured speaker over lunch or dinner -- would something like that be possible?

Best,
Aaron

-----Original Message-----
From: Rohrbaugh, Mark (NIH/OD) [E] [mailto:rohrbaum@od.nih.gov]
Sent: Wednesday, July 18, 2018 11:16 AM

To: Kesselheim, Aaron Seth,M.D.,M.P.H. <akesselheim@bwh.harvard.edu>
Subject: RE: Questions about CRADAs

External Email - Use Caution

Here is NIH's overview of CRADAs. https://www.ott.nih.gov/policy/cradas

-----Original Message-----
From: Kesselheim, Aaron Seth,M.D.,M.P.H. <akesselheim@bwh.harvard.edu>
Sent: Tuesday, July 17, 2018 10:43 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Subject: Questions about CRADAs

Hi Mark -- hope all is well. One of the people in my research group is doing a project on CRADAs and had a few fundamental questions that I thought you might be able to help with -- would it be ok to send the questions over email, or maybe set up a time to quickly chat?

Best,
Aaron

Aaron S. Kesselheim, M.D., J.D., M.P.H.
Associate Professor of Medicine at Harvard Medical School Director, Program On Regulation, Therapeutics, And Law (PORTAL) Division of Pharmacoepidemiology and Pharmacoeconomics Brigham and Women's Hospital
1620 Tremont St, Suite 3030
Boston MA 02120
akesselheim@partners.org
P: 617-278-0930; F: 617-232-8602
http://www.PORTALresearch.org

Faculty member, Harvard Medical School Center for Bioethics Irving S. Ribicoff Visiting Associate Professor of Law, Yale Law School (2016-2018) Editor-in-Chief, Journal of Law, Medicine, and Ethics

Don't miss our policy and ethics seminar series

The information in this e-mail is intended only for the person to whom it is addressed. If you believe this e-mail was sent to you in error and the e-mail contains patient information, please contact the Partners Compliance HelpLine at http://www.partners.org/complianceline . If the e-mail was sent to you in error but does not contain patient information, please contact the sender and properly dispose of the e-mail.

From: Berkson, Laura (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=ADB561AB47E54FDC94E2A54682514434-BERKSONLD]
Sent: 8/9/2017 8:20:04 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: A Chinese billionaire may get a monopoly on a cancer drug backed by U.S. taxpayers

Hey Mark,

I saw this article in STAT+ and wanted to flag it for you. Do you know if any other companies were interested in a license?

Laura

Laura Berkson, J.D.
Office of Legislative Policy & Analysis
National Institutes of Health
(301) 496-3471 | laura.berkson@nih.gov

A Chinese billionaire may get a monopoly on a cancer drug backed by U.S. taxpayers

By ED SILVERMAN @Pharmalot
AUGUST 9, 2017

The U.S. National Institutes of Health plans to award an exclusive license for promising medical technology that was funded by U.S. taxpayers to a company controlled by a Chinese billionaire.
In a notice posted on the Federal Register on Monday, the agency proposed giving patent rights for antibody drugs that would be used to treat liver cancer to Salubris Biotherapeutics, a division of a company that is largely owned by Ye Chenghai, a former mayor of Shenzhen, China, who is 51st richest person in China, according to Forbes.

This is only the latest in a string of such moves by the federal government to award exclusive licenses to technology that was developed with taxpayer dollars. And these proposals are generating intensifying criticism that the deals — which involve both domestic and foreign drug and vaccine makers — fail to ensure that the products will be sold at prices that are affordable for Americans.

Last week, Sen. Bernie Sanders (I-Vt.) proposed a rule that would force federal agencies and federally funded nonprofit institutions, including universities, to negotiate a reasonable pricing agreement before granting exclusive rights to make prescription drugs and vaccines. The amendment was floated amid a furor over a Zika virus vaccine that Sanofi (SNY) is developing with American taxpayer funding.

Lawmakers and consumer groups worry Sanofi, which has received $43 million in government research grants, will gain a monopoly through 2036 and its vaccine may not be affordable for many Americans. They point to some Sanofi drugs that are priced higher in the U.S. than elsewhere and want the Army to require Sanofi not to charge more in the U.S. than several other high-income countries. Sanofi denies rejecting an Army request for reasonable pricing.

"The fact that we're giving away taxpayer-funded research patent rights and not asking questions on pricing is odd, and it's even stranger when giving it to a foreign-owned company," said Jamie Love of Knowledge Ecology International, a consumer advocacy group that tracks intellectual property and access to medicines issues, and wrote the NIH to protest the license.

"I'm not saying you wouldn't want a foreign company involved in developing technology. But no matter who it is, you shouldn't give away technology without an agreement on pricing," he continued. "And in this case, we're just turning over intellectual property to a Chinese billionaire with no strings attached. It's an important technology and the benefits, if it works out, are significant."

Salubris Biotherapeutics, which is slated to receive the license and recently opened offices and a laboratory in Gaithersburg, Md., could not be reached for comment, nor could its parent company, Shenzhen Salubris Biotherapeutics (SHE:002294).

The advocacy group sent a letter asking the NIH to provide information about the terms of the proposed license, including royalties; how much funding was provided to the company by the government; and whether the license will include language that ensures that any drug based upon the patented invention will be "available to the public on reasonable terms" as required by federal law.

Uncertainty over such licenses last month prompted Sen. Angus King (I-Maine) to add an amendment to a Department of Defense spending bill to authorize the agency to exercise rights in a federal law which, under certain circumstances, would permit a company — other than the licensed patent holder — to make a lower-cost version of a drug. The Senate Armed Services Committee adopted the provision.

Also last month, Rep. Marcy Kaptur (D-Ohio) unsuccessfully introduced a similar amendment to a House appropriations bill that would have authorized the Department of Health and Human Services to take the same step. HHS oversees the NIH, by the way.

"This system is clearly broken. NIH's approval of this exclusive license does not appear to be in the interest of the American public," Kaptur said. "Our government needs to hold these drug makers accountable, and allowing foreign monopolies on drugs created with taxpayer money is an abuse of the public trust. Are we to expect that this company won't use its exclusive rights to price gouge consumers, as we have seen time and time again? This move by NIH is deeply concerning."

From: Joe Allen [jallen@allen-assoc.com]
Sent: 4/8/2016 7:49:42 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]; Hammersla, Ann (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=Recipients/cn=hammerslaa]
Subject: Drug shortage prompts concern that some are too cheap

Ever thought you'd see a story like this:
http://www.foxnews.com/health/2016/04/01/drug-shortages-prompt-question-are-some-medicines-too-cheap.html?intcmp=ob_article_sidebar_video&intcmp=obnetwork

If some were federally funded, perhaps KEI and Sen. Sanders could file a march in petition for the government to force an exclusive license so prices could be increased so they are accessible...

--

Joseph P. Allen
President
Allen and Associates
60704 Rt. 26, South
Bethesda, OH 43719
(W) 740-484-1814
(c) b6
www.allen-assoc.com

From: Jorgenson, Lyric (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/CN=RECIPIENTS/CN=JORGENSONLA]
Sent: 6/7/2017 2:27:00 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]
CC: Wolinetz, Carrie (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=Wolinetzcdc9a]; Fennington, Kelly (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=FENNINGTONKNEW]; Plude, Denise (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=Recipients/cn=parksde]
Subject: FW: WF 365590 - FYI
Attachments: 1a CRISPR-SecPrice-6Jan2017.pdf; Letter regarding DHHS policy on licensing of CRISPR patents

This one falls to Mark and Ann H, I believe. Mark can you develop/coordinate the response?

From: Plude, Denise (NIH/OD) [E]
Sent: Wednesday, June 07, 2017 10:24 AM
To: Jorgenson, Lyric (NIH/OD) [E] <jorgensonla@od.nih.gov>; Fennington, Kelly (NIH/OD) [E] <FenningK@OD.NIH.GOV>
Subject: WF 365590 - FYI

Work Folder Information
Work Folder: WF 365590
Process: FYI
Program Analyst: Boskent, Celeste (NIH/OD) [E]
Due Date:
WF Subject: Letter regarding DHHS policy on licensing of CRISPR patents.
IC: od_osp
From: Love, James
To: Collins, FrancisPrice, Tom
Remarks: GEN: FYI to OSP and NHGRI as Info only.

KNOWLEDGE ECOLOGY INTERNATIONAL

June 6, 2017

Dr. Thomas E. Price
Secretary
Department of Health and Human Services
200 Independence Avenue, S.W.
Washington, D.C. 20201
via email: Thomas.Price@hhs.gov

Dear Secretary Price:

Beginning in 2013, researchers — working on grants from the National Institutes of Health (NIH) — filed for a number of patents on **Clustered regularly interspaced short palindromic repeats** (**CRISPR**). The past two years there have been a number of patent applications filed and granted on CRISPR technologies, and also concerns about patents obstructing the advancement of science and about the development and pricing of new products including drugs and vaccines.

We are writing to ask the Department to develop a policy on the licensing of federally-funded CRISPR patented inventions.

In part 1, we review the importance of the CRISPR technology. Part 2 discusses the public interest in non-discriminatory licensing of CRISPR patent. In part 3, we make suggestions regarding the policies that would advance the public interest, and ensure that those inventions are "available to the public on reasonable terms"[1] and that the licenses are designed to achieve the purposes and objectives of the Bayh-Dole Act[2] and to maximize the benefits to taxpayers and patients.

---

[1] 35 USC § 201(f).

[2] 35 U.S.C. §§ 200 *et seq.*

Table of contents

Part 1. The CRISPR technology has important research and medical applications. 2

Figure 1: Pipeline of CRISPR–Cas- assisted drug discovery (From Fellmann C et al.) 6

Part 2. There is a public interest in open, non-discriminatory licensing of CRISPR patents on reasonable terms. 6

1. The CRISPR patent landscape and licensing arrangements. 6

Table 1: CRISPR patent landscape 7

Figure 2: CRISPR-CAS9 licensing agreements 9

2. Exclusive licenses on CRISPR are contrary to federal guidance 10

3. Exclusive licenses are an unnecessary and inappropriate means to incentivize research using the CRISPR platform. 11

4. Exclusive licenses on CRISPR patents will limit patient access. 11

Part 3. DHHS policy on the licensing of CRISPR patents. 12

Conclusion 14

Annex 1: NIH Sharing Policies and Related Guidance 15

Part 1. The CRISPR technology has important research and medical applications.

Our genes have been called the instruction manual to life. They determine everything from one's eye color to one's susceptibility to developing certain diseases. By being able to manipulate genes we could potentially correct the faulty ones that give rise to orphan diseases, such as spinal muscular atrophy, turn off genes that cause cancer, or even instruct our immune cells to destroy tumors.

Before CRISPR, editing genes was a very time consuming process that required complex systems, such as zinc fingers. When it came to whole organisms like mice, editing genes would take numerous rounds of breeding, many years, and a lot of luck. Even stably silencing genes in single cells could take several months using very common shRNA protocols.

What makes the CRISPR system superior is its simplicity, versatility, and precision. CRISPR is made of two components: the enzyme that cuts the gene, and the RNA template that instructs CRISPR where exactly to cut. Furthermore, this system can be used and adapted for any organism.

Gene editing is so essential to biomolecular research that the ramification of the CRISPR technology will touch every field of biology and medicine. Gene editing is used in virtually every biomedical lab and is among the first thing researchers teach their trainees to master (*i.e.*, using restriction enzymes, bacterial transformation, transfection, and site directed mutagenesis). Designing physiologically relevant organisms that model human diseases is a bedrock of medical research and drug discovery. Without these cellular and animal disease models, we cannot study disease mechanisms, nor could we screen vast libraries of molecules for potential medicines. There are already many gene-editing CRISPR tools and protocols demonstrating how to generate lentiviral CRISPR libraries or produce 'knock-out' animal models, such as in mice and fruit flies.[3, 4, 5, 6, 7]

The CRISPR-cas9 system is 4 years old and already we are seeing new innovations.[8, 9]

CRISPR technology has already been widely adopted by researchers, and "[a]pplications ... are appearing at a furious pace, and gathering momentum toward therapeutic use in human cells."[10] CRISPR is also "[f]aster, cheaper, and easier to use"[11] than older gene editing methods.

Scientists have also used the CRISPR technology to engineer mosquitoes to become resistant to malaria. This resistance is even passed to subsequent generations when the engineered mosquitoes mate with 'normal' (wild type) mosquitoes. This elegant solution not only prevents mosquitoes from spreading malaria, but also avoids exterminating an important food source for birds and other insectivores.[12]

HIV/AIDS could also be eradicated using CRISPR. HIV integrates into our genes, forcing people living with the virus to stay under treatment their whole lives. Currently, resources are directed towards eliminating HIV cellular reservoirs in the human body using, for example, HDAC inhibitors. However, with CRISPR, we could simply cut out pieces of the embedded viral

---

[3] Addgene CRISPR/Cas9 Guide. https://www.addgene.org/crispr/guide/

[4] Genetic Editing with CRISPR. https://research.cornell.edu/news-features/genetic-editing-crispr

[5] CRISPR-Cas: A Laboratory Manual. http://www.cshlpress.org/pdf/sample/2016/crispr-cas/CRISPR-CasFM.pdf

[6] CRISPR Genome Engineering Resources. http://www.genome-engineering.org/crispr/

[7] E-CRISP Design of CRISPR constructs. http://www.e-crisp.org/E-CRISP/

[8] Cong L et al. Multiplex genome engineering using CRISPR/Cas systems. Science. 2013 Feb 15;339(6121):819-23.

[9] Mali P et al. RNA-guided human genome engineering via Cas9.Science. 2013 Feb 15;339(6121):823-6.

[10] Caitlin Smith, "Editing the Editor: Genome Editing Gets a Makeover with CRISPR 2.0," *Science Magazine*, Jan. 13, 2017, http://www.sciencemag.org/custom-publishing/technology-features/editing-editor-genome-editing-gets-makeover-crispr-20.

[11] Id.

[12] Gantz VM et al. Highly efficient Cas9-mediated gene drive for population modification of the malaria vector mosquito Anopheles stephensi.Proc Natl Acad Sci U S A. 2015 Dec 8;112(49):E6736-43.

genome, forever silencing the virus.[13] Of course, this technology can be extended to other human viruses such as hepatitis B virus, human papillomavirus, and herpes virus.[14, 15, 16]

CRISPR had been used to knockout porcine endogenous retroviruses, making future transplants with porcine organs much safer, and thus addressing the shortage of organs for transplantation.[17] Proof of concept in animal models have already been published where CRISPR is used to remove genetic diseases such as Duchenne muscular dystrophy from germline DNA (sperm/egg).[18]

The CRISPR system is maturing quickly and its impact is stretching beyond biomedical research and into drug discovery and manufacturing. It promises to become as fundamental a molecular tool in drug development as the hammer is to building a house. When CRISPR is combined with current molecular tools such as high throughput functional screens, for example, CRISPR-cas9 can be adapted to comprehensively identify new cancer drug targets.[19] CRISPR based genomic screens (CRISPRi, CRISPRa) are also important in identifying disease mechanisms and epidemiological trends (polymorphisms).[20, 21]

Pharmaceutical giants such as Novartis, Bayer, and AstraZeneca have already adopted CRISPR technology into their drug discovery platforms for everything from cancer to blood disorders to blindness, and the technology is behind many new start ups.[22, 23, 24, 25, 26]

---

[13] Hu W. RNA-directed gene editing specifically eradicates latent and prevents new HIV-1 infection. Proc Natl Acad Sci U S A. 2014 Aug 5;111(31):11461-6.

[14] Wang J, Quake SR. RNA-guided endonuclease provides a therapeutic strategy to cure latent herpes viridae infection.Proc Natl Acad Sci U S A. 2014 Sep 9;111(36):13157-62.

[15] Kennedy EM et al. Inactivation of the human papillomavirus E6 or E7 gene in cervical carcinoma cells by using a bacterial CRISPR/Cas RNA-guided endonuclease. J Virol. 2014 Oct;88(20):11965-72.

[16] Kennedy EM et al. Suppression of hepatitis B virus DNA accumulation in chronically infected cells using a bacterial CRISPR/Cas RNA-guided DNA endonuclease.Virology. 2015 Feb;476:196-205.

[17] Yang L et al. Genome-wide inactivation of porcine endogenous retroviruses (PERVs).Science. 2015 Nov 27;350(6264):1101-4

[18] Long C et al. Prevention of muscular dystrophy in mice by CRISPR/Cas9-mediated editing of germline DNA. Science. 2014 Sep 5;345(6201):1184-8.

[19] Shi J et al. Discovery of cancer drug targets by CRISPR-Cas9 screening of protein domains. Nat Biotechnol. 2015 Jun;33(6):661-7

[20] Gilbert LA. Genome-Scale CRISPR-Mediated Control of Gene Repression and Activation. Cell. 2014 Oct 23;159(3):647-61.

[21] Shalem O, Sanjana NE, Zhang F. High-throughput functional genomics using CRISPR-Cas9. Nat Rev Genet. 2015 May;16(5):299-311.

[22] Novartis, CRISPR genome editing fuels cancer drug discovery. https://www.nibr.com/stories/nerd-blog/crispr-genome-editing-fuels-cancer-drug-discovery

[23]Megget K. Crispr goes commercial. Royal Society of Chemistry, Chemistry World. 2016https://www.chemistryworld.com/business/crispr-goes-commercial/9359.article

[24]Orcutt M. Big Pharma Doubles Down on CRISPR for New Drugs. MIT Technology Review. 2016. https://www.technologyreview.com/s/545366/big-pharma-doubles-down-on-crispr-for-new-drugs/)

[25] Swaminathan N. CRISPR-based startups are rushing to IPO and don't seem to care that we don't know who officially owns CRISPR, Quartz, 2016. https://qz.com/813552/crispr-therapeutics-ipo-raised-56-million-but-the-companys-future-is-in-jeopardy-because-of-the-crispr-patent-war/

Industries that rely on bacterial systems, such as in food processing (yogurt, cheese, etc.) or pharmaceutical and biofuel production (ethanol) may use CRISPR to make their bacterial stocks more resistant to contamination and increase productivity. [27]

Several clinical trials using CRISPR are set to begin in 2017 in the area of cancer immunotherapy.[28] Specifically, scientists in the United States and China are using CRISPR to engineer immune cells to fight cancer.[29]

Some have argued that CRISPR is spurring the kind of fruitful competition in R&D that has not been seen since the genome project, or even since Sputnik and the moon landing.[30]

CRISPR is a striking example of how allowing a broad or non-exclusive access to an essential technology can spur innovation at an incredible rate. Scientists, doctors and drug developers everywhere are already using and improving the CRISPR technology. Since 2013, over 4800 scientific articles related to CRISPR have appeared on pubmed. The impact of this technology parallels the sequencing of the human genome and engineering taq polymerase in PCR. Applying monopoly rights to such a fundamental tool will stifle innovation and slow down the progress to new and better medicines.

---

[26] Editas Medicine http://www.editasmedicine.com/, Intellia Therapeutics http://www.intelliatx.com/, Eligo Bioscience http://eligo-bioscience.com/, Autum https://www.atum.bio/ etc.

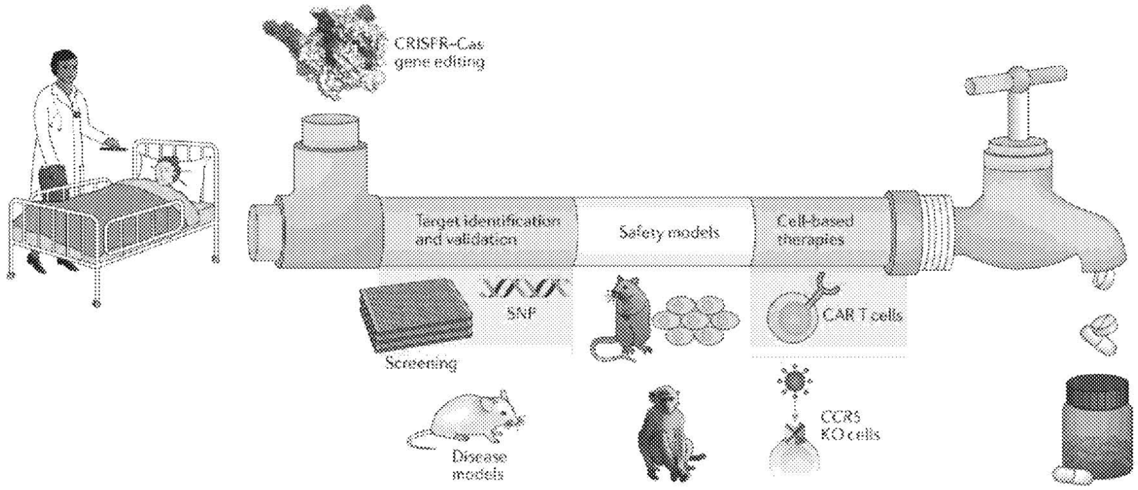
[27] Pak E. CRISPR: A game-changing genetic engineering technique. Harvard, Science in the News. 2014. http://sitn.hms.harvard.edu/flash/2014/crispr-a-game-changing-genetic-engineering-technique/

[28] First CRISPR clinical trial gets green light from US panel. http://www.nature.com/news/first-crispr-clinical-trial-gets-green-light-from-us-panel-1.20137

[29] CRISPR gene-editing tested in a person for the first time. http://www.nature.com/news/crispr-gene-editing-tested-in-a-person-for-the-first-time-1.20988?WT.mc_id=TWT_NatureNews

[30] China Has Launched the First-Ever CRISPR Gene-Editing Trial in Humans. http://fortune.com/2016/11/15/first-crispr-trial-humans-china/

Figure 1: Pipeline of CRISPR–Cas- assisted drug discovery (From Fellmann C *et al.*)[31]



Part 2. There is a public interest in open, non-discriminatory licensing of CRISPR patents on reasonable terms.

Patents on CRISPR cover the editing of over 20,000 genes in a variety of fields, from basic research to new cancer therapies. The use of exclusive licenses on the certain CRISPR technologies runs contrary to previous federal guidance, and aggressive licensing practices will harm the public by restricting research and development of new CRISPR technologies, hindering the development of products that use the inventions, and by increasing their prices.

1. The CRISPR patent landscape and licensing arrangements.

Key CRISPR patents are held by five universities, one hospital, and one researcher: Massachusetts General Hospital, Duke University, the Broad Institute (joint Harvard and Massachusetts Institute of Technology entity), the University of California, Berkeley, the University of Vienna, and Emmanuelle Charpentier (a French biologist, geneticist, and chemist), all of whom benefited from U.S. government research funding.

The Broad Institute, a joint venture between the Massachusetts Institute of Technology (MIT) and Harvard University, holds the following patents, invented by Feng Zhang in his Broad Institute laboratory:[32]

---

[31] Fellmann C, Gowen BG, Lin PC, Doudna JA, Corn JE.Cornerstones of CRISPR-Cas in drug discovery and therapy. Nat Rev Drug Discov. 2017 Feb;16(2):89-100.

[32] See here for additional information: http://keionline.org/node/2723.

Table 1: CRISPR patent landscape

Patent No.	Inventors	Assignees	Title	Filing Date
8697359	Feng Zhang	The Broad Institute; MIT	CRISPR-Cas systems and methods for altering expression of gene products	10/15/2013
8771945	Feng Zhang	The Broad Institute; MIT	CRISPR-Cas systems and methods for altering expression of gene products	2/18/2014
8795965	Feng Zhang	The Broad Institute; MIT	CRISPR-Cas component systems, methods and compositions for sequence manipulation	2/18/2014
8865406	Feng Zhang; Fei RAN	The Broad Institute; MIT	Engineering and optimization of improved systems, methods and enzyme compositions for sequence manipulation	3/24/2014
8871445	Le Cong; Feng Zhang	The Broad Institute; MIT; President and Fellows of Harvard College	CRISPR-Cas component systems, methods and compositions for sequence manipulation	4/23/2014
8889356	Feng Zhang	The Broad Institute; MIT	CRISPR-Cas nickase systems, methods and compositions for sequence manipulation in eukaryotes	2/18/2014
8895308	Feng Zhang; Fei RAN	The Broad Institute; MIT	Engineering and optimization of improved systems, methods and enzyme compositions for sequence manipulation	6/2/2014
8906616	Feng Zhang; Le Cong; Patrick Hsu; Fei RAN	The Broad Institute; MIT; President and Fellows of Harvard College	Engineering of systems, methods and optimized guide compositions for sequence manipulation	5/29/2014
8932814	Le Cong; Feng Zhang	The Broad Institute; MIT; President and Fellows of Harvard College	CRISPR-Cas nickase systems, methods and compositions for sequence manipulation in eukaryotes	4/22/2014
8945839	Feng Zhang	The Broad Institute; MIT	CRISPR-Cas systems and methods for altering expression of gene products	4/18/2014

8993233	Feng Zhang; Le Cong; Randall Jeffrey Platt; Neville Espi Sanjana; Fei RAN	The Broad Institute; MIT; President and Fellows of Harvard College	Engineering and optimization of systems, methods and compositions for sequence manipulation with functional domains	12/12/2013
8999641	Feng Zhang; Le Cong; Randall Jeffrey Platt; Neville Espi Sanjana	The Broad Institute; MIT; President and Fellows of Harvard College	Engineering and optimization of systems, methods and compositions for sequence manipulation with functional domains	3/26/2014

All of the Broad Institute patents declare government rights and funding in the inventions.

UC Berkeley has granted the rights in PCT/US2013/032589 (filed March 15, 2013) — claiming priority in the U.S. provisional applications 61/652,086 (filed May 25, 2012), 61/716,256 (filed Oct. 19, 2012), and 61/765,576 (filed Feb. 15, 2013) — and all following and related patent applications to Caribou Biosciences.[33] The recent interference proceedings at the Patent Trial and Appeals Board covered patent application 13/842,859 (filed March 15, 2013), which claims priority in all of the above U.S. patent applications.[34]

The CRISPR patents and patent applications are licensed for use in human therapeutics through three independent "surrogate" companies: Editas Medicine, Intellia Therapeutics, and CRISPR Therapeutics. Some of the universities directly license CRISPR technologies on nonexclusive terms for non-therapeutic use directly to researchers, while others have additional arrangements involving surrogates. The following figure from a recent article in *Science* by Jorge Contreras and Jacob Sherkow displays the relationships between patent holders, surrogates, and licensees, as well as the types of licenses:[35]

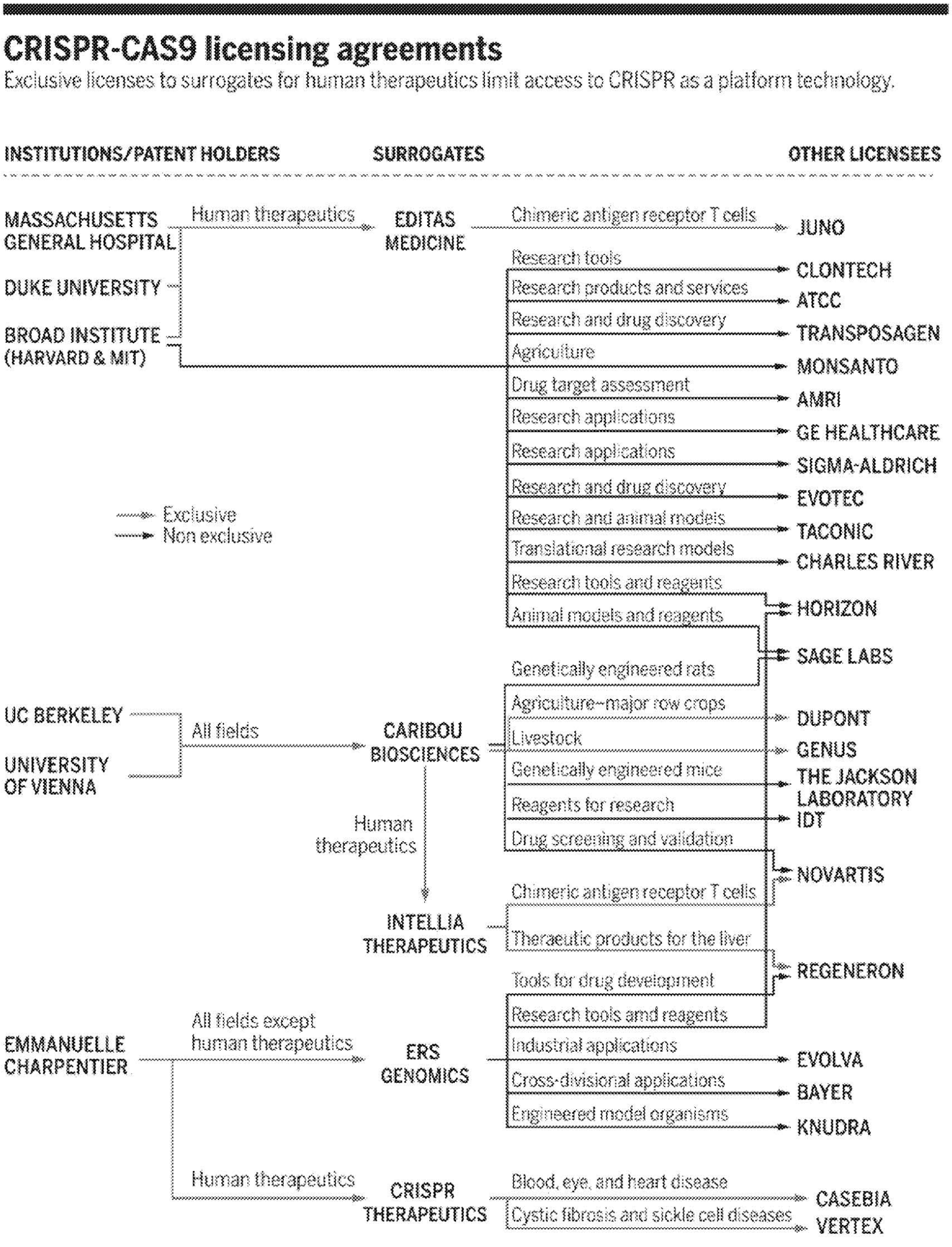
---

[33] Caribou Biosciences Exclusive License, https://dataverse.harvard.edu/file.xhtml?fileId=2970182&version=1.0.

[34] *Broad Inst. v. U.C. Regents*, Patent Interference No. 106,048 (P.T.A.B. Feb. 15, 2017) (per curiam), https://www.washingtonpost.com/news/speaking-of-science/wp-content/uploads/sites/36/2017/02/DecisionsOnMotions.pdf.

[35] Jorge L. Contreras and Jacob S. Sherkow, "CRISPR, Surrogate Licensing, and Scientific Discovery: Have Research Universities Abandoned Their Public Focus?," *Science* 355, no. 6326 (2017): 698-700.

Figure 2: CRISPR-CAS9 licensing agreements



CRISPR-CAS9 licensing agreements

Exclusive licenses to surrogates for human therapeutics limit access to CRISPR as a platform technology.

INSTITUTIONS/PATENT HOLDERS
SURROGATES
OTHER LICENSEES
MASSACHUSETTS GENERAL HOSPITAL
DUKE UNIVERSITY
BROAD INSTITUTE (HARVARD & MIT)
Human therapeutics
EDITAS MEDICINE
Chimeric antigen receptor T cells
JUNO
Research tools
CLONTECH
Research products and services
ATCC
Research and drug discovery
TRANSPOSAGEN
Agriculture
MONSANTO
Drug target assessment
AMRI
Research applications
GE HEALTHCARE
Research applications
SIGMA-ALDRICH
Research and drug discovery
EVOTEC
Research and animal models
TACONIC
Translational research models
CHARLES RIVER
Research tools and reagents
Animal models and reagents
HORIZON
SAGE LABS
Genetically engineered rats
Exclusive
Non exclusive
UC BERKELEY
UNIVERSITY OF VIENNA
All fields
CARIBOU BIOSCIENCES
Agriculture–major row crops
DUPONT
Livestock
GENUS
Genetically engineered mice
THE JACKSON LABORATORY
Reagents for research
IDT
Drug screening and validation
NOVARTIS
Human therapeutics
Chimeric antigen receptor T cells
INTELLIA THERAPEUTICS
Theraeutic products for the liver
Tools for drug development
REGENERON
EMMANUELLE CHARPENTIER
All fields except human therapeutics
ERS GENOMICS
Research tools amd reagents
Industrial applications
EVOLVA
Cross-divisional applications
BAYER
Engineered model organisms
KNUDRA
Human therapeutics
CRISPR THERAPEUTICS
Blood, eye, and heart disease
CASEBIA
Cystic fibrosis and sickle cell diseases
VERTEX

2. Exclusive licenses on CRISPR are contrary to federal guidance

The National Institutes of Health (NIH) issued a set of principles and practical guidance in 1999 for the recipients of NIH grants and contracts on the dissemination of "biomedical research resources,"[36] particularly research tools. Those principles contextualize the development of federally-funded biomedical research tools within the policy goals and obligations contained within the Bayh-Dole Act.

In interpreting the obligations of contractors under the Bayh-Dole Act, the NIH explained the obligation of federally-funded researchers to ensure broad access to research tools:

> "Generally, recipients are expected to maximize the use of their research findings by making them available to the research community and the public, and through their timely transfer to industry for commercialization."[37]

Moreover, they noted that the right of federal contractors to retain title to federally-funded obligations entailed "corresponding obligations to promote utilization, commercialization, and public availability of these inventions."[38]

However, the NIH warned against the use of exclusive licenses as the primary means for promoting utilization, commercialization, and public availability in the context of research tools:

> "Where the subject invention is useful primarily as a research tool, inappropriate licensing practices are likely to thwart rather than promote utilization, commercialization and public availability of the invention."[39]

CRISPR is a "broadly applicable 'platform' technology — like stem cells or the internet — that could enable innumerable specific applications."[40] The patents on CRISPR held by the universities, as noted above, cover the editing of 20,000-plus genes in the human genome, and are not directed to specific fields of use. The grant of exclusive licenses on the use of CRISPR technologies for use in broad fields of research — such as cancer therapeutics, liver diseases, and agricultural uses — runs contrary to the NIH guidance on the appropriate use of licenses to advance biomedical research and development.

---

[36] National Institutes of Health, Principles and Guidelines for Recipients of NIH Research Grants and Contracts on Obtaining and Disseminating Biomedical Research Resources, 64 Fed. Reg. 72090 (Dec. 23, 1999).
[37] Id. at 72092.
[38] Id. at 72092.
[39] Id. at 72092-93.
[40] Contreras and Sherkow, 700.

3. Exclusive licenses are an unnecessary and inappropriate means to incentivize research using the CRISPR platform.

The widespread use of CRISPR on nonexclusive terms provides ample evidence that exclusive licenses on the gene editing tools are unnecessary to incentivize use, or research using the editing tools.

Of the licensing agreements identified by Sherkow and Contreras, three quarters (21 out of 28) have been on nonexclusive terms, with two companies receiving both exclusive and nonexclusive licenses.

An HHS advisory committee comprised of top public health officials and clinical researchers has also recognized that scientists have independent incentives — apart from patents and exclusive licenses — to conduct biomedical research, particularly in the area of genetic research, including the "desire to advance understanding, help their patients by developing treatments for disease, advance their careers, and enhance their reputations."[41]

Exclusive licenses are inappropriate in promoting the development of CRISPR technologies because they "could rapidly bottleneck the use of CRISPR technology to discover and develop useful human therapeutics,"[42] as well as technologies in other fields. Sherkow and Contreras argued that broad licensing agreements — for example, in the field of Chimeric Antigen Receptor T cell (CAR-T) cancer immunotherapy, which Juno Therapeutics has an exclusive license on from Editas Medicine — could prevent the use of CRISPR for research in areas where the exclusive licensee does not have the bandwidth to develop the technology, particularly in the field of rare disease drugs.[43]

4. Exclusive licenses on CRISPR patents will limit patient access.

The HHS advisory committee found that monopoly conditions on genetic test technologies have resulted in higher prices and limited patient access. For example, exclusivities on the BRCA cancer test and the Canavan disease genetic test resulted in higher prices above a competitive market rate. In the case of the BRCA test, the high prices have created barriers to the use of the test, or the timely use of the test, even for high risk patients. The Canavan patent holder "used their patent monopoly to establish restrictive license conditions and sought license fees that exceeded what laboratories offering similar tests for Tay-Sachs disease were willing to pay."[44]

---

[41] Secertary's Advisory Committee on Genetics, Health, and Society, Department of Health and Human Services, Gene Patents and Licensing Practices and Their Impact on Patient Access to Genetic Tests (2010), 20, http://osp.od.nih.gov/sites/default/files/SACGHS_patents_report_2010.pdf (hereinafter "Secretary's Advisory Committee Report").

[42] Contreras and Sherkow, 698.

[43] Contreras and Sherkow, 700.

Clinical access was also limited by the licensing practices of patent holders on genetic tests,[45] and, in cases where "an exclusive-rights holder narrowed or cleared the market of competing tests through patent enforcement,"[46] patients also faced limited access. For example, the patent holders for tests for the hearing loss gene *GJB2* and for familial LQTS have used their monopoly rights to force competitors out of the market.[47]

CRISPR has application both in genetic testing and in therapeutics. Exclusive licenses on fundamental CRISPR patents coupled with aggressive licensing practices will create problems.

Part 3. DHHS policy on the licensing of CRISPR patents.

As noted in Annex 1, DHHS has adopted at least 20 statements on sharing policies and related guidance for NIH-funded research resources.

There is a pressing need for a U.S. government policy statement regarding the licensing of government-funded CRISPR inventions.

The following comments are offered to assist the DHHS in developing such a policy statement:

1. In 2001 and in subsequent agreements with the WiCell Research Institute, Inc., the NIH intervened to ensure access to non-commercial research institutions to patented inventions involving stem cells.[48] The WiCell/NIH agreement can be seen as implementing a 1999 NIH policy statement on "Sharing Biomedical Research Resources,"[49] and focused primarily on ensuring non-profit entities would be able to use stem cells for research purposes.[50]

---

[44] Secretary's Advisory Committee Report, 38.
[45] Id., 39-42.
[46] Id., 42.
[47] Id., 42-45.
[48] WiCell Agreement No. 02-W012B, 09042012 NIH, Amended and Restated Memorandum of Understanding between WiCell Research Institute, Inc. and Public Health Service U.S. Department of Health and Human Services. November 2012. https://www.ott.nih.gov/sites/default/files/documents/pdfs/wicell-rev.pdf.
[49] National Institutes of Health. Sharing Biomedical Research Resources: Principles and Guidelines for Recipients of NIH Research Grants and Contracts. Federal Register Vol. 64, No. 246, page 72090-6. December 23, 1999.
[50] Debra Roberton, NIH sacrifices commercial rights in WiCell deal, *Nature Biotechnology* 19, 1001 (1 November 2001), doi:10.1038/nbt1101-1001.

2. The policy statement for CRISPR patents should ensure non-exclusive licensing in all fields of technology. The CRISPR technology is not a product, but a tool that can be used to create products and advance our understanding of human diseases. It is in the public interest to ensure non-discriminatory freedom to use the technology, in some cases royalty-free, and in other cases with fair and reasonable remuneration.

3. A related area concerns patents that are essential to implement standards. For many technologies, including but not limited to those involving networked information technologies or green energy technologies, so-called standards essential patents (SEPs) can impose costs on society and limit innovation, if licensed on unreasonable or discriminatory terms. Often these disputes are resolved through contracts between patent holders and Standards Developing Organizations (SDOs), with a commitment that the patent holders agree to license patents on fair, reasonable, and non-discriminatory terms, referred to as FRAND terms. The US Patent and Trademark Office (USPTO) and the U.S. Department of Justice (USDOJ) have addressed this issue in a nuanced January 8, 2013 policy statement.[51]

4. In the case of the CRISPR patents, the policy should be to ensure open and non-discriminatory licensing of the patents to both nonprofit and for-profit entities.

5. The licensing of CRISPR patents to non-commercial entities for research purposes should be royalty-free, a condition met by earlier CRISPR patent holders.

6. The licensing of CRISPR patents to commercial entities may require payment of royalties, but only on FRAND terms.

7. The licensing of CRISPR patents to any entity should not have reach-through rights to subsequent patents, unless the reach-through clause is designed to benefit an entity that is creating a research commons.

8. The funding agency should require the patent holders to disclose license agreements and royalty payments, as well as the rationale for royalties charged.

9. The NIH should reserve the right to require that royalty payments be based upon only the use as a research tool, or only on final products.

---

[51] United States Department Of Justice And United States Patent & Trademark Office Policy Statement On Remedies For Standards-essential Patents Subject To Voluntary F/rand Commitments January 8, 2013

Conclusion

We thank you for your attention to this important issue, and request a meeting to discuss this matter further at your convenience.

Sincerely,

James Love

James Love, Director
Knowledge Ecology International (KEI)
james.love@keionline.org
+1.202.332.2670

Diane Singhroy
Scientific and Technical Advisor
Knowledge Ecology International
diane.singhroy@keionline.org

Andrew S. Goldman, Esq.
Counsel, Policy and Legal Affairs
Knowledge Ecology International
+1.202.332.2670
andrew.goldman@keionline.org

Cc: Francis Collins, M.D., PhD. Director, National Institutes of Health.

Annex 1: NIH Sharing Policies and Related Guidance

It is NIH policy that the results and accomplishments of the activities that it funds should be made available to the public. PIs and funding recipient institutions are expected to make the results and accomplishments of their activities available to the research community and to the public at large. The following links highlight selected NIH policies and related guidance on sharing of research resources developed with NIH funding.

1. Policy on Dissemination of NIH-Funded Clinical Trial Information (8/2016)
2. NIH Intramural Human Data Sharing Policy (8/2016)
3. NIH Public Access Plan for Increasing Access to Scientific Publications and Digital Scientific Data from NIH Funded Scientific Research (02/2015) (PDF - 474 KB) – This document describes NIH's plans to build upon and enhance its longstanding efforts to increase access to scholarly publications and digital data resulting from NIH-funded research.
4. Genomic Data Sharing (GDS) (8/2014) Final Genomic Data Sharing (GDS) Policy that provides for the sharing, for research purposes, of large-scale human and non-human genomic data generated from NIH-funded research. Effective for grant applications and contract proposals submitted for January 25, 2015 due date and thereafter.
5. NIH Grants Policy Statement (Availability of Research Results) (11/2015) - Section of the NIH Grants Policy Statement discussing the availability of research results developed with NIH funding, including publications, data, unique research resources, and intellectual property (inventions and patents).
6. Common Data Element (CDE) Resource Portal (03/2013) - The Common Data Element (CDE) Resource Portal provides access to NIH-supported CDE initiatives and other tools and resources which can help researchers use common data elements (CDEs) in clinical research, patient registries, and other human subject research in order to improve data quality and opportunities for comparison and combination of data from multiple studies and with electronic health records.
7. Table of NIH Data Sharing Policies (03/2013) - This table lists additional data sharing policies in effect at NIH at the NIH, IC, division, and program levels that apply to broad sets of investigators and data.
8. Table of NIH Data Sharing Repositories (03/2013) - This table lists various NIH-supported data repositories that accept submissions of appropriate data from NIH-funded investigators and others, as well as including resources that aggregate information about biomedical data and information sharing systems.
9. Data Repositories Resource Guide (09/2012) - (MS Word - 30 KB) - This resource guide document is designed to assist the NIH extramural community by identifying examples of data repositories which may be used for sharing data developed under NIH funding programs, consistent with NIH sharing policies.

10. Data Standards and Common Data Elements Resource Guide (09/2011) - (MS Word - 29 KB) - This resource guide document is designed to assist the NIH extramural community in identifying and utilizing certain data standards and common data elements in NIH programs.
11. Example Plan addressing Key Elements for a Data Sharing Plan under NIH Extramural Support (08/2010) - (MS Word - 55 KB) - This resource document is designed to assist the NIH extramural applicant community in preparing data sharing plans by providing an example that shows how a sharing plan addresses the key elements for a data sharing plan.
12. Key Elements to Consider in Preparing a Data Sharing Plan under NIH Extramural Support (12/2009) – (PDF - 32 KB) - This resource document is designed to assist the NIH extramural applicant community in preparing data sharing plans by identifying key elements that should be addressed in the plan.
13. NIH Genome-Wide Association Studies (GWAS) Policy (Policy for Sharing of Data Obtained in NIH Supported or Conducted Genome-Wide Association Studies (GWAS)) (08/2007) - Policy concerning sharing of GWAS data obtained in NIH supported or conducted research. (Please refer to Genomic Data Sharing (GDS) Policy webpage.)
14. Data Sharing Regulations/Policy/Guidance Chart for NIH Awards (08/30/2006) - (MS Word - 62 KB) - This chart is designed as a quick guide only for the purpose of identifying various data sharing regulation/policy/guidance documents applicable to NIH funding.
15. NIH Public Access Policy (02/2005) - Policy on Enhancing Public Access to Archived Publications Resulting from NIH-Funded Research.
16. NIH Model Organism Sharing Policy (NIH Policy on Sharing of Model Organisms for Biomedical Research) (05/2004) - Policy concerning the sharing and distributing of model organisms and related research resources generated using NIH funding.
17. NIH Data Sharing Policy (Final NIH Statement on Sharing Research Data) (02/2003) - Policy concerning the sharing of research data for funding applications seeking $500,000 or more in direct costs in any year of the project period.
18. NIH Research Tools Policy (Principles and Guidelines for Recipients of NIH Research Grants and Contracts on Obtaining and Disseminating Biomedical Research Resources) (12/1999) - (PDF – 150 KB) - Policy designed to provide NIH funding recipients with guidance concerning appropriate terms for disseminating and acquiring unique research resources developed with federal funds, and intended to assist recipients in complying with their obligations under the Bayh-Dole Act and NIH funding policy.
19. Biological Materials Policy (NIH Procedures for Handling Non-Election of Title to Patentable Biological Materials) (05/1996) - NIH policy for allowing NIH funding recipients to retain and license biological materials for which patent protection might not be pursued.
20. Developing Sponsored Research Agreements (Considerations for Recipients of NIH Research Grants and Contracts) (11/1994) - Issues and points to consider in developing sponsored research agreements with commercial entities, where such agreements may include research activities which are fully or partially funded by NIH, in

order to assist funding recipients ensure such agreements comply with the requirements of the Bayh-Dole Act and NIH funding agreements while upholding basic principles of academic freedom.

From: jamespackardlove@gmail.com [jamespackardlove@gmail.com]
on behalf of Jamie Love [james.love@keionline.org]
Sent: 6/5/2017 6:22:51 PM
To: Collins, Francis (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=Collinsfr]; Price, Thomas (HHS/OS) [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=D76b3edcd55c49e29c9361e5073a5fef-Price, Thomas E. (OS]
CC: Andrew S. Goldman [andrew.goldman@keionline.org]; Diane Singhroy [diane.singhroy@keionline.org]; Claire Cassedy [claire.cassedy@keionline.org]; Manon Ress [manon.ress@keionline.org]; Thiru Balasubramaniam [thiru@keionline.org]
Subject: Letter regarding DHHS policy on licensing of CRISPR patents
Attachments: CRISPR-SecPrice-6Jan2017.pdf

Dear Secretary Price and NIH Director Francis Collins,

Attached is a letter from KEI asking DHHS to develop a policy on the licensing of CRISPR patents.

James Love
Director
Knowledge Ecology International

--
James Love. Knowledge Ecology International
http://www.keionline.org/donate.html
KEI DC tel: +1.202.332.2670, US Mobile: +1.202.361.3040, Geneva Mobile: +41.76.413.6584,
twitter.com/jamie_love

From: Rogers, Karen (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=B23EF4CA2FA14A6EB174EE611953A396-ROGERSK]
Sent: 7/18/2018 3:39:14 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]

Subject: FW: TDC-Short July Meeting
Attachments: CRADA-License Overlap.pptx; Triaging NIH Technology Transfer Information Requests.pptx
Location: Web-Ex dial-in info, Agenda, presentations below

Start: 7/18/2018 3:30:00 PM
End: 7/18/2018 5:00:00 PM
Show Time As: Tentative

-----Original Appointment-----
From: Gadhia, Ami (NIH/NCATS) [E]
Sent: Wednesday, July 11, 2018 10:39 AM
To: Gadhia, Ami (NIH/NCATS) [E]; NIH TDC Short
Cc: Campbell, Eggerton (NIH/NHGRI) [E]; Conley, Vio (NIH/NCI) [E]; Koelble, Peg (NIH/NHLBI) [E]; Carroll, Kathleen (NIH/NCI) [E]; Balakrishnan, Krishna (NIH/NCATS) [E]; Amar, Anna (NIH/NCI) [E]; Rogers, Karen (NIH/OD) [E]; Roering, Jill (NIH/OD) [E]; Guyton, Nicole (NIH/NCI) [E]; Leff, Michelle (NIH/NIDA/IRP) [E]; Stackhouse, Thomas (NIH/NCI) [E]; Portilla, Lili (NIH/NCATS) [E]; Tilotta, Sally (NIH/NIEHS) [E]; Solowiej, Anna (NIH/NHGRI) [E]; Bailey, Brian (NIH/NHLBI) [E]; Rohrbaugh, Mark (NIH/OD) [E]; Driscoll, Claire (NIH/NHGRI) [E]; Goodwin, Rebecca (NIH/NLM/LHC) [E]; Maurey, Karen (NIH/NCI) [E]; Wong, Jennifer (NIH/NIMH) [E]; Gunas, Heather (NIH/NCI) [E]; Saeger, David (NIH/CC/OD) [E]
Subject: TDC-Short July Meeting
When: Wednesday, July 18, 2018 11:30 AM-1:00 PM (UTC-05:00) Eastern Time (US & Canada).
Where: Web-Ex dial-in info, Agenda, presentations below

TDC-Short **Meeting Agenda**
Wednesday, July 18th, 11:30 am – 1:00 pm

Join meeting in my Webex Personal Room
b6

Join by phone
1-650-479-3208 Call-in toll number (US/Canada)
Access code: b6
Global call-in numbers

---

1. **Topics for Discussion:**

a. Summary of Patent Legal Services (PLS) Contract workgroups. Jeff Thomas and Maryann Puglielli.

b. Discuss new report on returning individual research results to participants that was released by NAS recently. Anna Amar.

c. Triaging policy issues and TT questions from various sources. Mark Rohrbaugh and Karen Rogers.

d. Discuss documentation of CRADAs and how OTT can help. Karen Rogers.

e. Multi-party IIA template agreement. Ami Gadhia.

2. **Upcoming:**

a. The next TDTC Forum will be on August 6th.

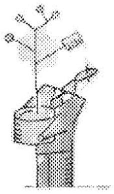
b. Contact Ami Gadhia and Surekha Vathyam with agenda topics for both meetings.

CRADA-License Overlap.pptx

Triaging NIH Technology Tran...

License Royalties Linked to CRADAs

Karen Rogers
Acting Director, OTT
July 18, 2018



b5

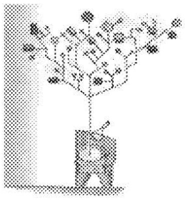
b5

b5

b5

b5

Triaging NIH Technology Transfer Information Requests



Mark Rohrbaugh

Special Advisor for Technology Transfer

Karen Rogers

Acting Director, Office of Technology Transfer

b5

b5

b5

b5

b5

From: Shmilovich, Michael (NIH/NHLBI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7DFE19BFD1D443CEB700B9F22D159A90-SHMILOVM]
Sent: 8/28/2018 1:23:42 PM
To: Deutch, Alan (NIH/NHLBI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=244d755700584812af36b5e787285647-deutcha]; Berkley, Dale (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5ee461c29f5045a49f0adf82caaa2f31-berkleyd]; Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: FW: Sinotau and MTTI licenses
Attachments: KEI-UACT-NIH-MTTI-27Aug2018.pdf; NIH to KEI re MTTI 27Aug2018.docx

Dale, Mark and Alan -- ...same for MTTI... please review.

From: James Love <james.love@keionline.org>
Sent: Monday, August 27, 2018 16:57
To: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>
Cc: Luis Gil Abinader <luis.gil.abinader@keionline.org>; Claire Cassedy <claire.cassedy@keionline.org>; Manon Ress <MANON.RESS@cancerunion.org>
Subject: Sinotau and MTTI licenses

Michael Shmilovich, Esq.
Senior Licensing and Patent Manager
National Heart, Lung and Blood Institute
National Institutes of Health
31 Center Drive
Room 4A29, MSC2479
Bethesda, MD
Email: shmilovm@mail.nih.gov

Dear Michael Shmilovich

Attached are two comments filed jointly by KEI and UACT, regarding licenses noticed in the federal register.

1. Prospective Grant of Exclusive Patent License: Radiotherapy for Metastatic Castration-Resistant Prostate Cancer, 83 FR 35667 (www.federalregister.gov/d/2018-16066)

2. Prospective Grant of Exclusive Patent License: Radiotherapeutics Against Somatostatin-Receptor Expressing Neuroendocrine Tumors, 83 FR 35663 (https://www.federalregister.gov/d/2018-16065)

James Love

--
James Love. Knowledge Ecology International
http://www.keionline.org
twitter.com/jamie_love

August 27, 2018

Michael Shmilovich, Esq.
Senior Licensing and Patent Manager
National Heart, Lung and Blood Institute
National Institutes of Health
31 Center Drive
Room 4A29, MSC2479
Bethesda, MD
Email: shmilovm@mail.nih.gov

RE: Prospective Grant of Exclusive Patent License: Radiotherapeutics Against Somatostatin-Receptor Expressing Neuroendocrine Tumors, 83 FR 35663 (https://www.federalregister.gov/d/2018-16065)

Dear Michael Shmilovich:

Knowledge Ecology International and the Union for Affordable Cancer Treatment (UACT) are writing to provide comments on the prospective grant of an exclusive patent license for a radiotherapeutic against neuroendocrine tumors that express somatostatin receptors to Molecular Targeting Technologies, Inc. (MTTI), a Delaware corporation.

According to the Federal Register notice, the prospective patent license will be granted "worldwide" and for a field of use "not broader than radiotherapeutics for somatostatin-receptor expressing neuroendocrine tumors."

According to the Delaware Department of State Division of Corporations, MTTI was incorporated on December 20, 2001. As described on their website, "MTTI is a privately held biotechnology company translating novel radiopharmaceuticals for disease treatment and diagnosis."[1] The co-founder and CEO of MTTI is Koon Yan "Chris" Pak, Ph.D.

Dr. Pak has previously worked with Centocor and has served as the President of the Chinese American Society of Nuclear Medicine, the Vice Chair of the Global Monte Jade Science and Technology Association, and the Chairman of the Chinese Entrepreneur Association which he co-founded.[2]

MTTI currently has several therapeutics and diagnostics indications in their pipeline.[3]

The Federal Register notice 83 FR 35663 describes the invention as follows:

---

[1] https://web.archive.org/web/20180808003041/http://www.mtarget.com/
[2] https://web.archive.org/web/20180826003534/http://www.mtarget.com/ABUS.html
[3] https://web.archive.org/web/20180826034052/http://www.mtarget.com/PIPE.html

> The invention pertains to a radiotherapeutic against neuroendocrine tumors that express somatostatin receptor. Radionuclide therapies directed against tumors that express somatostatin receptors (SSTRs) have proven effective for the treatment of advanced, low- to intermediate-grade neuroendocrine tumors. The subject radiotherapeutic covered by the subject patent estate includes a somatostatin (SST) peptide derivative like octreotate (TATE), conjugated to an Evans Blue (EB) analog, and further chelated via DOTA to therapeutic radionuclide177 Lu, a beta emitter. The EB analog reversibly binds to circulating serum albumin and improves the pharmacokinetics of SST peptide derivatives and reduce peptide-receptor radionuclide therapy toxicity. EB analog conjugated to octreotate (EB-DOTATATE) has been shown by the inventors to provide reversible albumin binding in vivo and extended half-life in circulation. When EB-TATE is slowly released into the tumor microenvironment, tumor uptake and internalization into SSTR positive tumors resulted in delivery of radioactive particles and tumor cell killing. EB-TATE displayed significantly more favorable pharmacokinetics than TATE alone by achieving higher tumor to non-tumor penetration as evidenced by positron emission tomography.

A Clinicaltrials.gov search for the term "EB-TATE" reflects that there are at least 2 clinical trial studies recruiting that relate to EB-TATE for the treatment of neuroendocrine tumors[4]. These two clinical studies are identified as NCT03308682 and NCT03478358. These two studies received funding from the NIH and are co-sponsored by the Peking Union Medical College Hospital and the NIH's National Institute for Biomedical Imaging and Bioengineering (NIBIB), according to Clinicaltrials.gov. Both are Phase 1 studies, started in April 30, 2017 and their estimated completion date is May 1, 2018 (NCT03308682) and August 1, 2018 (NCT03478358). Their estimated enrollment is 30 participants (NCT03308682), and 20 participants (NCT03478358), respectively.

https://docs.google.com/spreadsheets/d/1zfprL_CelaGQ8BExHPUzslnahVQdXNk40nQfA5Wi33U/edit?usp=sharing

The Federal Register notice 83 FR 35663 only describes one patent document, the International Patent Application PCT/US2017/054863 filed October 3, 2017. This is a very recent application and, at the time this comment is being filed, this patent document does not appear published in the WIPO PatentScope database nor other patent databases. A patent search based on the phrase "Evans Blue Derivatives and Their Use As Radiotherapy" returns one PCT document filed by the NIH with Xiaoyuan Chen and Orit Jacobson Weiss as inventors, but identified with the International Patent Application No. PCT/US2017/031696, which is different from the patent document described in the Federal Register notice 83 FR 35663. The lack of clear and publicly available information regarding the actual scope of the invention claimed in the application that the NIH plans to license to MTTI undermines the general public's ability to comment on this prospective exclusive license.

---

[4] https://clinicaltrials.gov/ct2/results?cond=EB-TATE&term=&cntry=&state=&city=&dist=&Search=Search

Moreover, according to the Federal Register notice 83 FR 35663 in addition to the International Patent Application PCT/US2017/054863, the prospective exclusive license will include "all continuing U.S. and foreign patents/patent applications thereof." The Federal Register notice does not explain how many additional "continuing U.S. and foreign" applications the NIH has filed or plans to file based on the same priority number, nor whether the NIH plans to start the national PCT phase for this invention in developing countries. In order to analyze whether in this case an exclusive license is a reasonable and adequate incentive consistent with the statutory requirements of 35 USC § 209, and to properly respond to the Federal Register notice, it is necessary to have complete information on the actual geographical scope of the prospective exclusive license, and to have a discussion of the role of government agencies in funding research related to the invention, and the expected costs of bringing a new treatment to market. The notice 83 FR 35667 does not contain such information.

At this point, KEI opposes the granting of an exclusive license, on the grounds that the NIH have not provided sufficient information to evaluate a request for an exclusive license.

However, in the event that the NIH does issue an exclusive license, we propose several conditions on the exclusive license to ensure that the benefits of the invention are available to the public on reasonable terms,[5] and that the scope of the exclusive rights are limited to that which are reasonably necessary to induce the investment necessary to achieve practical application of the invention.[6]

1. No discrimination against US residents in pricing

We ask that the NIH include language in the proposed exclusive license to ensure that the prices in the U.S. for any drug, vaccine, medical device or other health technology using the inventions are not higher than the median price charged in the seven countries with the largest gross domestic product (GDP), that also have a per capita income of at least 50 percent of the United States, as measured by the World Bank Atlas Method.

We consider this a modest request to protect U.S. residents, who paid for the R&D that created the licensed inventions.

2. Reduce term of exclusivity when revenues are large

In addition to an external reference pricing test, we propose that the exclusivity of the license in the U.S. should be reduced when the global cumulative sales from products or services using the inventions exceed certain benchmarks.

---

[5] Required by 35 USC § 201(f).
[6] 35 USC § 209.

Given the modest cost of acquiring an NIH patented invention, the amount of money the developer needs in sales to justify additional investments in R&D is reduced, as compared to cases where a company developes or acquires the technology from non government sources.

This request is consistent with the statutory requirements of 35 USC § 209, which requires that "the proposed scope of exclusivity is not greater than reasonably necessary to provide the incentive for bringing the invention to practical application."

One possible implementation of revenue benchmarks is as follows: exclusivity will be reduced by one year for every $500 million in revenue equivalents, earned after the first $1 billion, where revenue equivalent is defined as global cumulative sales plus market entry rewards as well as government grants or tax credits, for the product or products using the invention. However, the NIH could choose different benchmarks, so long as the limits on exclusivity address the requirements of 35 USC 209, that the incentive is "not greater than reasonably necessary."

3. Developing countries

We are concerned that several NIH-funded inventions are not accessible in developing countries, due to prices that are high and not affordable in markets where per capita incomes are significantly lower than the United States. For this reason, we ask the NIH to limit the exclusivity in the license to countries that have per capita incomes that are at least 30 percent of the United States.

We also ask the NIH to reach out to the Medicines Patent Pool (MPP), in order to enter into an agreement that gives the MPP an option to negotiate non-exclusive open licenses for the inventions in developing countries.

4. Transparency

The licensee should be required to file an annual report to the NIH, available to the public, on the research and development (R&D) costs associated with the development of any product that uses the inventions, including reporting separately and individually the outlays on each clinical trial. We will note that this is not a request to see a company business plan or license application. We are asking that going forward the company be required to report on actual R&D outlays to develop the subject inventions. Reporting on actual R&D outlays is important for determining if the NIH is meeting the requirements of 35 USC § 209, that "the proposed scope of exclusivity is not greater than reasonably necessary to provide the incentive for bringing the invention to practical application." Specifically, having data on actual R&D outlays on each clinical trial used to obtain FDA approval provides evidence that is highly relevant to estimating the risk adjusted costs of bringing NIH licensed inventions to market.

Sincerely,

James Love
james.love@keionline.org
Knowledge Ecology International (KEI)
https://keionline.org

Luis Gil Abinader
luis.gil.abinader@keionline.org
Knowledge Ecology International (KEI)

Manon Anne Ress
Manon.Ress@cancerunion.org
Union for Affordable Cancer Treatment (UACT)
https://uact.org

b5

b5

b5

From: Mowatt, Michael (NIH/NIAID) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=CB1EF7E2E54B4164AE34814574BDA638-MMOWATT]
Sent: 8/23/2017 12:44:40 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
CC: Mowatt, Michael (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cb1ef7e2e54b4164ae34814574bda638-mmowatt]; Frisbie, Suzanne (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c402740ceaad4d4f97a8c28f16fbb349-frisbies]
Subject: RE: Week Ahead
Attachments: OSP Week Ahead Report 08-28-2017 NIAID REQUEST 170822.docx; Korch memo White Paper publication DRAFT 170806 8.8.17 2pm.pdf; Vax Strat Plan 4.14.17 Exec Summ - version 8.5.2017 1pm - response.docx

Mark,

Here's the summary I worked out with John Mascola, Hilary Marston, and JJ. Tony has it as well.

I've also attached the draft memo from ASPR and the White Paper.

Please give me a call to confirm next steps: b6

Including Suzanne for her awareness.

Thanks very much for your help with this priority project!

Mike

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Wednesday, August 16, 2017 12:41 PM
To: Mowatt, Michael (NIH/NIAID) [E] <mmowatt@niaid.nih.gov>
Subject: Fwd: Week Ahead

Mike:

To get the Zika license issue on the table for NIH to talk to the HHS policy people, we need a summary of the issue in this week a head sample attached. b5 b5

Sent from my iPhone

Begin forwarded message:

> **From:** "Bayha, Ryan (NIH/OD) [E]" <bayhar@od.nih.gov>
> **Date:** August 16, 2017 at 12:35:46 PM EDT
> **To:** "Rohrbaugh, Mark (NIH/OD) [E]" <rohrbaum@od.nih.gov>
> **Subject: Week Ahead**
>
> Hi Mark,
>
> Here is the week ahead template. I need this to me by Friday COB to get into next week's report which covers Aug 28-Sept 1.

Thanks
Ryan

**Ryan T.
Bayha
Director of Strategic Engagement
Office of Science Policy
National Institutes of Health
6705 Rockledge Drive, Suite 750
Bethesda, MD 20892
301- 496-9838 (p)
301-496-9839 (f)**

**Subscribe to "Under the Poliscope" NIH OSP's new blog!
Follow OSP on Twitter @CWolinetzNIH**

NIH Week Ahead Report – Office of Science Policy (OSP) Submission

Week of 08/28/2017

- Item:

  Category: Non-Routine

  Action Needed By: ASAP, preferably 09/01/2017

b5

b5

b5

b5

b5

From: Marshall, Lisa (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/CN=OD/CN=SCHWARTZL]
Sent: 4/7/2016 2:41:09 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]
CC: Plude, Denise (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=Recipients/cn=parksde]; Carr, Sarah (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=CARRS]
Subject: RE: Xtandi letter (fr KEI)

Yes, I just received OER clearance of this letter (without comments). So, you have all the comments for the congressional letter. Were you going to try to get me a draft today? Thanks, Lisa

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Thursday, April 07, 2016 10:37 AM
To: Marshall, Lisa (NIH/OD) [E]
Cc: Plude, Denise (NIH/OD) [E]; Carr, Sarah (NIH/OD) [E]
Subject: RE: Xtandi letter (fr KEI)

Lisa:

Do I have all the comments now for the letter from HHS to Congress on the public meeting?

Thanks,
Mark

From: Marshall, Lisa (NIH/OD) [E]
Sent: Thursday, April 07, 2016 10:04 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Cc: Plude, Denise (NIH/OD) [E] <pludede@mail.nih.gov>; Carr, Sarah (NIH/OD) [E] <CarrS@OD.NIH.GOV>
Subject: FW: Xtandi letter (fr KEI)

Hi Dr. Rohrbaugh,
Here are clearance comments from OGC on the Xtandi march-in letter. I'm assuming that we will not send this response until the congressional response has been sent, correct? Sorry about my confusion. Also, OS Exec Sec advised me that they aren't really in a position to clear this letter (since FC is signing) and that we should only include it as background when we send the final draft of the response for the Secretary's signature.

From: Hammersla, Ann (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/CN=RECIPIENTS/CN=HAMMERSLAA]
Sent: 4/24/2017 7:24:20 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]
Subject: RE: WF 357204 - Response Creation due 5/1

FC as recommended by ML

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, April 24, 2017 3:23 PM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Subject: RE: WF 357204 - Response Creation due 5/1

Exec Sec asks who should sign it. **b5**

From: Hammersla, Ann (NIH/OD) [E]
Sent: Monday, April 24, 2017 3:15 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Subject: RE: WF 357204 - Response Creation due 5/1

Thanks. I have not received this yet. Ann

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Monday, April 24, 2017 2:54 PM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Subject: FW: WF 357204 - Response Creation due 5/1

In case you did not get it through ES yet...

From: Plude, Denise (NIH/OD) [E]
Sent: Monday, April 24, 2017 2:52 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Cc: Wertz, Jennifer (NIH/OD) [E] <wertzj@od.nih.gov>
Subject: WF 357204 - Response Creation due 5/1

Work Folder Information
Work Folder: WF 357204
Process: Response Creation
Program Analyst: Hurlebaus, Lisa (NIH/OD) [E]
Due Date: May 01, 2017
WF Subject: OS assignment. KEI & UACT write about the prostate cancer drug, Xtandi (enzalutamide). Asks the Government to reconsider the decision not to use the 'march-in' rights, under the Bayh-Dole Act, for this excessively-priced drug. (AS-760889)
IC: od_osp
From: Goldman, Andrew
To: Price, TomMattis, Jim
Remarks: OS assignment. Note to OER & OSP: Please work together to prepare Direct Reply response. You should decide/recommend who should sign draft response (Dr. Lauer or Dr. Wolinetz; or someone else?). Please provide draft response to Exec Sec in DDRMS by 12:00pm, Monday, May 1, for OD clearances. Thanks very much, Lisa Hurlebaus

---

From: Rodriguez, Richard (NIH/NCI) [E] [/O=NIH/OU=EXTERNAL (FYDIBOHF25SPDLT)/CN=RECIPIENTS/CN=5C43750192CA4E0E890422519477DD41]
Sent: 6/6/2017 6:49:09 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]
CC: Berkley, Dale (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=BERKLEYD]; Rucker, Susan (NIH/NCI) [E] [/O=NIH/OU=EXTernal (FYDIBOHF25SPDLT)/cn=Recipients/cn=ac50fd0447444c2e9666d65287a9af2f]; Maurey, Karen (NIH/NCI) [E] [/O=NIH/OU=EXTernal (FYDIBOHF25SPDLT)/cn=Recipients/cn=918c32b0a9174941a3d2807a3ec25c2d]
Subject: RE: Broad CRISPR patents

A call would be good and I'm looping Karen Maurey in.

Thanks

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Tuesday, June 06, 2017 2:02 PM
To: Rucker, Susan (NIH/NCI) [E] <susan.rucker@nih.gov>
Cc: Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>; Berkley, Dale (NIH/OD) [E] <BerkleyD@OD.NIH.GOV>
Subject: RE: Broad CRISPR patents

Yes, we should probably talk about this b5 b5 b5 I will look at the apps in TTS. Thx. Can we talk maybe next week? Who should be on the call besides us? Anyone?

From: Rucker, Susan (NIH/NCI) [E]
Sent: Tuesday, June 06, 2017 1:54 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Cc: Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>; Berkley, Dale (NIH/OD) [E] <BerkleyD@OD.NIH.GOV>
Subject: RE: Broad CRISPR patents

Mark:

b5

Is this enough information for now?

I don't know of any others.

Susan S. Rucker, JD, CLP
Senior Advisor for Intellectual Property Transactions

Technology Transfer Center
National Cancer Institute
NCI Shady Grove
9609 Medical Center Drive
Room 1E-530, MSC 9702
Bethesda, MD 20892-9702

Phone: 240.276.6727
Fax: 240.276.5504
E-mail: susan.rucker@nih.gov

This e-mail may contain confidential and/or privileged material for the sole use of the intended recipient. Any review or distribution by others is strictly prohibited. If you are not intended recipient please contact the sender and delete all copies of this e-mail.

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Tuesday, June 06, 2017 9:38 AM
To: Rucker, Susan (NIH/NCI) [E] <susan.rucker@nih.gov>
Cc: Rodriguez, Richard (NIH/NCI) [E] <richard.rodriguez@nih.gov>; Mowatt, Michael (NIH/NIAID) [E] <MMOWATT@niaid.nih.gov>; Berkley, Dale (NIH/OD) [E] <BerkleyD@OD.NIH.GOV>
Subject: Broad CRISPR patents

Susan:

Do you know of any CRISPR patents or applications with NIH inventors? Dale said he thought you might be aware of one from Broad with an NLM inventor.

Thanks,
Mark

Mark L. Rohrbaugh, Ph.D., J.D.
Special Advisor for Technology Transfer
Director, Division of Technology Transfer and Innovation Policy
Office of Science Policy
Office of the Director
National Institutes of Health

From: Vepa, Sury (NIH/NCATS) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=25B6C29F123544738FCBAD51627B2D23-VEPAS]
Sent: 7/11/2018 2:26:28 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Portilla, Lili (NIH/NCATS) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=9b03f548be224eb9b7b6167a32e9cc4a-portilll]; Alvarez, Mayra (NIH/NCATS) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=966dc355bf5a4efca30a542e28d8064a-alvarezlope]
Subject: RE: Prospective Grant of Exclusive Patent License: Mutant IDH1 Inhibitors Useful for Treating Cancer to Apexx Oncology. Notice for comment published in 83 FR 29562.

Mark,

Thanks. I will request my colleague, Mayra to send you the call in information for 3 .30PM today, if it still works for you.

Regards,

Sury

Phone: 301-827-7181
Cell: b6
E-Mail: sury.vepa@nih.gov

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Tuesday, July 10, 2018 4:57 PM
To: Vepa, Sury (NIH/NCATS) [E] <sury.vepa@nih.gov>; Portilla, Lili (NIH/NCATS) [E] <portilll@mail.nih.gov>
Subject: RE: Prospective Grant of Exclusive Patent License: Mutant IDH1 Inhibitors Useful for Treating Cancer to Apexx Oncology. Notice for comment published in 83 FR 29562.

I have time until 5:30 today or tomorrow after 3. Does that work?

From: Vepa, Sury (NIH/NCATS) [E]
Sent: Tuesday, July 10, 2018 4:42 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; Portilla, Lili (NIH/NCATS) [E] <portilll@mail.nih.gov>
Subject: Fwd: Prospective Grant of Exclusive Patent License: Mutant IDH1 Inhibitors Useful for Treating Cancer to Apexx Oncology. Notice for comment published in 83 FR 29562.

Mark and Lili, I would like to discuss with you on how to respond to another email from KEI (see below) asking for more detailed information. Please let me know your availability for a brief call. Mark, if you think we can do this by email, please advise. Thanks, Sury

Sent from my iPhone

Begin forwarded message:

> **From:** James Love <james.love@keionline.org>
> **Date:** July 10, 2018 at 4:35:07 PM EDT
> **To:** "Vepa, Sury (NIH/NCATS) [E]" <sury.vepa@nih.gov>
> **Cc:** Luis Gil Abinader <luis.gil.abinader@keionline.org>, Claire Cassedy <claire.cassedy@keionline.org>, Manon Ress <manon.ress@keionline.org>, Thiru Balasubramaniam <thiru@keionline.org>

Subject: Re: Prospective Grant of Exclusive Patent License: Mutant IDH1 Inhibitors Useful for Treating Cancer to Apexx Oncology. Notice for comment published in 83 FR 29562.

July 10, 2018

Sury Vepa, Ph.D., J.D.,
Senior Licensing and Patenting Manager,
National Center for Advancing Translational Sciences
National Institutes of Health
Email sury.vepa@nih.gov

Re: Prospective Grant of Exclusive Patent License: Mutant IDH1 Inhibitors Useful for Treating Cancer to Apexx Oncology. Notice for comment published in 83 FR 29562.

https://www.federalregister.gov/documents/2018/06/25/2018-13486/prospective-grant-of-exclusive-patent-license-mutant-idh1-inhibitors-useful-for-treating-cancer

Dear Dr. Vepa,

Knowledge Ecology International (KEI) offers the following comments on the, "Prospective Grant of Exclusive Patent License: Mutant IDH1 Inhibitors Useful for Treating Cancer," to Apexx Oncology, which was noticed in the Federal Register (83 FR 29562).

As far as the public can determine, Apexx Oncology is a secretive startup company. The only information we could find using a Google search about the company was a contest for a logo of the company. There is no record of a registered trademark for Apexx Oncology with the USPTO. No web page has been located. It is not obvious if Apexx Oncology is a new name for GeneXion Oncology (as indicated today), or a new company entirely, and in any case, there is next to nothing generally known about the company under either name.

When the NIH proposes giving an exclusive license on a patent to a company for which almost nothing is known, it should provide at the very least some basic information about the company. In seeking to respond to the first FR notice in this case, we had asked if GeneXion was owned by a company in Switzerland, but the NIH declined to answer. We don't know who is on the board of directors, who the key staff are or if another company owns this company. We would like to know if any current or former NIH employees or contractors are part of the company.

We also seek to learn -- why this company was selected in the first place? Do they have people who have worked on this particular technology, or have some special expertise? And since the patents are fairly new, did the NIH have no reasonable prospects for a license to an entity with more resources and a stronger track record than a company that seems to barely exist?

Here are some general provisions that we recommend for an exclusive license by the NIH.

1. **No discrimination against US residents in pricing.**

Prices in the U.S. for any drug, vaccine, medical device or other health technology using the invention should not be higher than the median price charged in the seven countries with the largest gross domestic product (GDP), that also have a per capita income of at least 50 percent of the United States, as measured by the World Bank Atlas Method.

2. **Developing countries.**

The license should not be exclusive for countries with a per capita income that is less than 30 percent of the US.

3. **Transparency.**

The licensee should be required to file an annual report to the NIH, available to the public, on the research and development (R&D) costs associated with the development of any product that uses the invention, including reporting separately and individually the outlays on each clinical trial. We will note that this is not a request to see a company business plan or license application. We are asking that going forward the company be required to report on actual R&D outlays to develop the subject inventions.

4. **Reduce term of exclusivity when revenues are large.**

The exclusivity of the license in the U.S. should be reduced by one year for every $500 million in revenue equivalents, earned after the first $1 billion, where revenue equivalent is defined as global cumulative sales plus market entry rewards as well as government grants or tax credits, for the product or products using the invention.

Sincerely,

James Love
Knowledge Ecology International
james.love@keionline.org
https://keionline.org

--

James Love. Knowledge Ecology International
http://www.keionline.org/donate.html
KEI DC tel: +1.202.332.2670, US Mobile: +1.202.361.3040, Geneva Mobile: +41.76.413.6584,
twitter.com/jamie_love

From: Shmilovich, Michael (NIH/NHLBI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7DFE19BFD1D443CEB700B9F22D159A90-SHMILOVM]
Sent: 8/28/2018 3:42:28 AM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Berkley, Dale (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5ee461c29f5045a49f0adf82caaa2f31-berkleyd]
CC: Deutch, Alan (NIH/NHLBI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=244d755700584812af36b5e787285647-deutcha]
Subject: FW: Sinotau and MTTI licenses
Attachments: KEI-UACT-NIH-Sinotau-27Aug2018.pdf; NIH to KEI re Sinotau 27Aug2018.docx

Mark, Dale and Alan – enclosed please find KEI and Cancer Union's response to our FR publication giving notice of our intent to grant an exclusive license to Sinotau in the field of radiotherapy for metastatic castration resistant prostate cancer. b5

Thanks again,

Michael A. Shmilovich, Esq., CLP
National Heart, Lung, and Blood Institute
Office of Technology Transfer and Development
31 Center Drive Room 4A29, MSC2479
Bethesda, MD 20892-2479
o. 301.435.5019
shmilovm@nih.gov

This message may contain privileged and confidential information intended only for the use of the individual(s) or entity named above. If you are not the intended recipient, you are hereby notified that any use, dissemination, distribution, or copying of this message or its content is strictly prohibited. If you have received this message in error, please notify sender immediately and destroy the message without making a copy. Thank you.

From: James Love <james.love@keionline.org>
Sent: Monday, August 27, 2018 17:06
To: Shmilovich, Michael (NIH/NHLBI) [E] <michael.shmilovich@nih.gov>
Cc: Luis Gil Abinader <luis.gil.abinader@keionline.org>; Claire Cassedy <claire.cassedy@keionline.org>; Manon Ress <MANON.RESS@cancerunion.org>
Subject: Re: Sinotau and MTTI licenses

Michael, the version of the Sinotau comments previously send was not the final version, and I sent it my mistake. It should be this file. If you can delete the previous one, which has very few differences, but this one has Luis as a co-signature, and he did most of the work.

Jamie

On Mon, Aug 27, 2018 at 4:57 PM, James Love <james.love@keionline.org> wrote:

> Michael Shmilovich, Esq.
> Senior Licensing and Patent Manager
> National Heart, Lung and Blood Institute
> National Institutes of Health
> 31 Center Drive

Room 4A29, MSC2479
Bethesda, MD
Email: shmilovm@mail.nih.gov

Dear Michael Shmilovich

Attached are two comments filed jointly by KEI and UACT, regarding licenses noticed in the federal register.

1. Prospective Grant of Exclusive Patent License: Radiotherapy for Metastatic Castration-Resistant Prostate Cancer, 83 FR 35667 (www.federalregister.gov/d/2018-16066)

2. Prospective Grant of Exclusive Patent License: Radiotherapeutics Against Somatostatin-Receptor Expressing Neuroendocrine Tumors, 83 FR 35663 (https://www.federalregister.gov/d/2018-16065)

James Love

--
James Love. Knowledge Ecology International
http://www.keionline.org
twitter.com/jamie_love

--
James Love. Knowledge Ecology International
http://www.keionline.org
twitter.com/jamie_love

August 27, 2018

Michael Shmilovich, Esq.
Senior Licensing and Patent Manager
National Heart, Lung and Blood Institute
National Institutes of Health
31 Center Drive
Room 4A29, MSC2479
Bethesda, MD
Email: shmilovm@mail.nih.gov

RE: Prospective Grant of Exclusive Patent License: Radiotherapy for Metastatic Castration-Resistant Prostate Cancer, 83 FR 35667 (www.federalregister.gov/d/2018-16066)

Dear Michael Shmilovich:

Knowledge Ecology International (KEI) and the Union for Affordable Cancer Treatment (UACT) are writing to provide comments on the prospective grant of an exclusive patent license for the commercialization of radiotherapeutics for metastatic castration-resistant prostate cancer to Sinotau Pharmaceutical Group, headquartered in Beijing, China, as noticed in the Federal Register notice 83 FR 35667 (www.federalregister.gov/d/2018-16066).

According to the Surveillance, Epidemiology, and End Results (SEER) program in the National Cancer Institute (NCI) Division of Cancer Control and Population Sciences (DCCPS), prostate cancer is the second leading cause of death from cancer for men.[1] In 2015, 3.1 million men were estimated to be living with prostate cancer. The estimated number of deaths from prostate cancer for 2018 is 29,430, and is estimated to account for 4.8 percent of all deaths from cancer. [2]

African-Americans are more than twice as likely to die from prostate cancer than men of other racial and ethnic groups. [3]

---

[1] https://web.archive.org/web/20180816015209/https://seer.cancer.gov/statfacts/html/prost.html

[2] *Ibid.*

[3] In African American men, the incidence of prostate cancer is almost 60 % higher and the mortality rate is two to three times greater than in Caucasians. Shenoy, Divya et al. “Do African-American Men Need Separate Prostate Cancer Screening Guidelines?” BMC Urology 16 (2016): 19. PMC. Web. 27 Aug. 2018. ""https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4862049/; NIH and Prostate Cancer Foundation launch large study on aggressive prostate cancer in African-American men. July 17, 2018. https://www.nih.gov/news-events/news-releases/nih-prostate-cancer-foundation-launch-large-study-aggressive-prostate-cancer-african-american-men; Ina Wu and Charles S. Modlin, Disparities in prostate cancer in African American men: What primary care physicians can do
Cleveland Clinic Journal of Medicine. 2012 May;79(5):313-320..

In the past, federally-funded inventions for the treatment of cancer have been available in the United States at prices significantly higher than the prices of the same treatment in other high income countries. For example, the current GoodRx price for one year of the prostate cancer drug enzalutamide, when sold by Astellas under the brand name of Xtandi, is $151,037 ($103.46 per 40 mg capsule) retail, or $136,035 ($93.17 per 40 mg capsule), using the GoodRx coupon. By contrast, the price of Xtandi outside the US in another typical high income country is far lower. For example, in Australia, Xtandi is 33.07AUD per capsule[4], equal to $24.29 per 40 mg capsule, or $35,463 per year.

Prices for the drug are generally unaffordable in developing countries and are sometimes even higher in developing countries than in Europe.[5] As a consequence, access to this drug which is easy to administer is often severely limited in the developing world, leading to unnecessary premature deaths and suffering, an outcome that should be problematic for at least some government officials.

According to the notice in the Federal Register, the prospective exclusive license "would be granted worldwide" and for a field of use "not broader than radiotherapeutics for metastatic castration-resistant prostate cancer," the same indication as Xtandi.

Sinotau Pharmaceutical Group was founded in 2004.[6] The Sinotau Pharmaceutical Group has several subsidiaries, including one called Sinotau Radiopharmaceutical which, according to the Sinotau Group's website, "is focused on development of a neurologic precision diagnostics pipeline with a focus on neurodegenerative diseases, oncology and other relevant afflictions."[7] According to the Sinotau Group's website, in 2016, "Sinotau Group and Enigma Biomedical Group, a Canadian company, formed Cerveau Technologies, Inc., in Boston (USA), to help the global development of Sinotau's Radiopharmaceutical pipeline."[8] Cerveau has signed exclusive license agreements for the development and commercialization of medical technologies with other pharmaceutical companies, including Merck and FluoroPharma Medical Imaging, Inc.[9]

The Federal Register notice 83 FR 35667 describes the invention as follows:

> "The invention covered by the patents and patent applications pertaining to HHS Ref. No. E-054-2018-0 pertain to a therapeutic agent that includes a chemically conjugated residue derived from (((R-)-1-carboxy-2-mercaptoethyl)carbamoyl)-L-glutamic acid that is further bound to an Evans blue analog (EB). The EB analog reversibly binds to circulating serum albumin to provide a radiopharmaceutical that retains affinity and

---

[4] https://web.archive.org/web/20180827191518/http://www.pbs.gov.au/medicine/item/10174L

[5] Additional price comparisons here. https://docs.google.com/spreadsheets/d/1pNGEybsksMVZ_hZnVKVjS2lrjC2aAnwlyNw5ghSg_us/edit#gid=1908943673

[6] https://web.archive.org/web/20180827151941/http://www.sinotau.com/english/about.html

[7] https://web.archive.org/web/20180827151941/http://www.sinotau.com/english/about.html

[8] https://web.archive.org/web/20180827151941/http://www.sinotau.com/english/about.html

[9] https://web.archive.org/web/20180827153520/http://www.sinotau.com/english/news.html

> specificity to prostate specific membrane antigen (PSMA; in this case PSMA-617). PSMA is a surface molecule shown to be specifically expressed by prostate tumor cells. PSMA expression levels correlate with disease stage and with hormone refractory cancers. Although most PSMA expression appears to be restricted to the prostate cancer, low levels of expression can also be detected in the brain, kidneys, salivary glands, and small intestine. The antigen is also shown to be expressed by neovascular tumor vessels of multiple other cancers. Inclusion of the Evans blue analog promotes high internalization and retention rates of the conjugated target ligand, and therefore, higher accumulation in PSMA positive tumors. Labeling EB-PSMA-617 derivatives with the therapeutic beta emitters, e.g.,90 Y,86 Y, and 177 Lu gives rise to improved tumor response and survival rates."

A Clinicaltrials.gov search for "PSMA-617" reflects that there are at least 8 clinical trial studies recruiting or recently launched related to PSMA-617 for the treatment of prostate cancer.[10]

At least one of those studies, NCT03403595[11], received funding from NIH project 1ZIAEB000073-08.[12] NCT03403595 is a Phase 1 study that started on December 1, 2017 and its estimated completion date is December 1, 2018. The estimated enrollment is 30 participants. The same NIH funded project also listed 9 other clinical trials as being related.[13]

The Federal Register notice 83 FR 35667 only describes one patent document, U.S. Provisional Patent Application 62/633,648 filed February 22, 2018. This is a very recent application that does not appear in the USPTO or other patent databases and has likely not yet been published pursuant to 35 USC § 122. The lack of public information regarding the actual scope of the invention claimed in the application that the NIH plans to license to Sinotau Pharmaceutical Group undermines the general public's ability to comment on this prospective exclusive license.

Moreover, according to the Federal Register notice 83 FR 35667, in addition to the U.S. Provisional Patent Application 62/633,648 the prospective exclusive license will include "all continuing U.S. and foreign patents/patent applications thereof." Nevertheless, the Federal Register notice does not explain how many additional "continuing U.S. and foreign" applications the NIH has filed or plans to file based on the priority application 62/633,648, nor whether the NIH plans to file applications claiming this invention in developing countries.

In order to analyze whether in this case an exclusive license is a reasonable and adequate incentive consistent with the statutory requirements of 35 USC § 209, and properly respond to the Federal Register notice, it is necessary to have more information on the actual geographical scope of the prospective exclusive license, the role of government agencies in funding research related to the invention, and the expected costs of bringing a new treatment to market. The notice 83 FR 35667 does not contain such information, even though this is essential for making the analysis required by § 209.

---

[10] https://clinicaltrials.gov/ct2/results?cond=PSMA-617+&term=&cntry=&state=&city=&dist=

[11] https://clinicaltrials.gov/ct2/show/NCT03403595

[12] https://projectreporter.nih.gov/project_info_details.cfm?aid=9555654&icde=40913634

[13] https://projectreporter.nih.gov/project_info_ct.cfm?aid=9555654&icde=40913634

At this point, KEI and UACT oppose the granting of an exclusive license, on the grounds that the NIH have not provided sufficient information to evaluate a request for an exclusive license.

However, in the event that the NIH does issue an exclusive license, we propose several conditions on the exclusive license to ensure that the benefits of the invention are available to the public on reasonable terms[14], and that the scope of the exclusive rights are "not greater than reasonably necessary to provide the incentive for bringing the invention to practical application." [15]

1. No discrimination against US residents in pricing

We ask that the NIH include language in the proposed exclusive license to ensure that the prices in the U.S. for any drug, vaccine, medical device or other health technology using the inventions are not higher than the median price charged in the seven countries with the largest gross domestic product (GDP), that also have a per capita income of at least 50 percent of the United States, as measured by the World Bank Atlas Method.

We consider this a modest request to protect U.S. residents, who paid for the R&D that created the licensed inventions.

2. Reduce term of exclusivity when revenues are large

In addition to an external reference pricing test, we propose that the exclusivity of the license in the U.S. should be reduced when the global cumulative sales from products or services using the inventions exceed certain benchmarks.

Given the modest cost of acquiring an NIH patented invention, the amount of money the developer needs in sales to justify additional investments in R&D is reduced, as compared to cases where a company develops or acquires the technology from non government sources.

This request is consistent with the statutory requirements of 35 USC § 209, which demands that "the proposed scope of exclusivity is not greater than reasonably necessary to provide the incentive for bringing the invention to practical application."

One possible implementation of revenue benchmarks is as follows: exclusivity will be reduced by one year for every $500 million in revenue equivalents, earned after the first $1 billion, where revenue equivalent is defined as global cumulative sales plus market entry rewards as well as government grants or tax credits, for the product or products using the invention. However, the

---

[14] Required by 35 USC § 201(f).

[15] 35 USC § 209.

NIH could choose different benchmarks, so long as the limits on exclusivity address the requirements of 35 USC § 209, in that the incentive is "not greater than reasonably necessary."

3. Developing countries

We are concerned that several NIH-funded inventions are not accessible in developing countries, due to prices that are high and not affordable in markets where per capita incomes are significantly lower than the United States. For this reason, we ask the NIH to limit the exclusivity in the license to countries that have per capita incomes that are at least 30 percent of the United States.

We also ask the NIH to reach out to the Medicines Patent Pool (MPP), in order to enter into an agreement that gives the MPP an option to negotiate non-exclusive open licenses for the inventions in developing countries.

4. Transparency

The licensee should be required to file an annual report to the NIH, available to the public, on the research and development (R&D) costs associated with the development of any product that uses the inventions, including reporting separately and individually the outlays on each clinical trial. We will note that this is not a request to see a company business plan or license application. We are asking that going forward the company be required to report on actual R&D outlays to develop the subject inventions. Reporting on actual R&D outlays is important for determining if the NIH is meeting the requirements of 35 USC § 209, that "the proposed scope of exclusivity is not greater than reasonably necessary to provide the incentive for bringing the invention to practical application." Specifically, having data on actual R&D outlays on each clinical trial used to obtain FDA approval provides evidence that is highly relevant to estimating the risk adjusted costs of bringing NIH licensed inventions to market.

Sincerely,

James Love
james.love@keionline.org
Knowledge Ecology International (KEI)
https://keionline.org

Luis Gil Abinader
luis.gil.abinader@keionline.org
Knowledge Ecology International (KEI)

Manon Anne Ress
Manon.Ress@cancerunion.org
Union for Affordable Cancer Treatment (UACT)
https://uact.org

b5

b5

b5

From: Joe Allen [jallen@allen-assoc.com]
Sent: 12/18/2016 10:13:43 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]
Subject: Re: Comment replying to me

I'd heard that, what about the impact on licensing?

On 12/16/2016 10:16 PM, Rohrbaugh, Mark (NIH/OD) [E] wrote:

> NIH reported that number of CRADAs increased several fold after language was dropped
>
> Sent from my iPhone
>
> On Dec 16, 2016, at 9:36 PM, Joe Allen <jallen@allen-assoc.com> wrote:
>
>> Thanks, what was the impact of introducing the language on NIH exclusive licensing? If there was an impact (hopefully negative) that would be a very interesting topic to explore.
>>
>> Have a great weekend!
>>
>> On 12/16/2016 5:09 PM, Rohrbaugh, Mark (NIH/OD) [E] wrote:
>>
>>> The clause in CRADAs and in all exclusive licenses was concurrent. People often talk of it as if it was only used in CRADAs but it was both. The broader issue was discussed publicly and rescinded at the same time under Dr. Varmus. The press release in April 1995 mentions both in the first sentence .
>>>
>>> **From:** Joe Allen [mailto:jallen@allen-assoc.com]
>>> **Sent:** Friday, December 16, 2016 4:21 PM
>>> **To:** Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
>>> **Subject:** Re: Comment replying to me
>>>
>>> 1992? That seems really late for NTIS licensing NIH inventions. The problem is that this is a precedent the other side will seize upon. It's surprising that companies accepted such a clause in their license. Wasn't this the same time that Congress was pressuring you to include "reasonable pricing" language in NIH CRADAS? As discussed yesterday, this is the first I've heard of anything like this in a license. The only way to make lemonade out of this (as far as I can see) is to look at how such a clause impacted NIH licensing. If we can show a decline and subsequent rise after it was removed, that would certainly bolster the cause. Still, this language will probably come back to bite us from our pals at KEI.

You said you got a call from a reporter. Was it about this language in NIH licensing agreements? If so, the cat's out of the bag.

Anyway, enjoy the weekend. Even with rain at least we'll get above freezing, which seems pretty alluring right now...

On 12/16/2016 12:12 PM, Rohrbaugh, Mark (NIH/OD) [E] wrote:

> b6 It seemed to have evolved. Just a quick survey...couldn't find it in a few late 80s agreements I looked at but found this clause in 1992 NTIS agreement. It does not use the term "practical application" like B-D
>
> <mime-attachment.jpg>
>
> **From:** Joe Allen [mailto:jallen@allen-assoc.com]
> **Sent:** Thursday, December 15, 2016 11:21 AM
> **To:** Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
> **Subject:** Re: Comment replying to me
>
> Wow, never knew that . We had some really contentious meetings with our Deputy Assistant Secretary when I argued after passage of the FTTA that agencies shouldn't be forced to license through CUFT (Center for the Utilization of Federal Technology) at NTIS. They really fought that as they realized that if they had to compete they would go out of business (which they did). So they were putting reasonable pricing clauses in exclusive licenses? Do you have one you could send me? No wonder they were so ineffective. Do you think Norm Latker knew those clauses were being put into exclusive licenses for NIH inventions? I wonder how many were licensed with that provision
>
> I learn something every day (and this is one thing I hate to have learned)...
>
> On 12/15/2016 11:03 AM, Rohrbaugh, Mark (NIH/OD) [E] wrote:
>
>> Yes it was in all exclusive licenses and it may have started with Licenses coming out of Commerce before NIH took them over
>>
>> Sent from my iPhone

On Dec 15, 2016, at 10:11 AM, Joe Allen <jallen@allen-assoc.com> wrote:

> Are we talking about the "reasonable pricing" language that NIH was pressured into using for CRADAS and later withdrew? If so, I didn't know it was extended to exclusive licenses for NIH inventions (and would have objected that such actions were not sanctioned under the law if I had known).
>
> On 12/14/2016 8:15 PM, Rohrbaugh, Mark (NIH/OD) [E] wrote:
>
>> Right,and it was not just CRADAs,it was all exclusive licenses
>>
>> Sent from my iPhone
>>
>> On Dec 14, 2016, at 7:59 PM, Joe Allen

<jallen@allen-assoc.com> wrote:

I would say that the answer is that Congress in pressur ingNIHtoincludereasonablepricingrequirementsinCRADAS was acknowledging that the term as used in the definition didn 't apply to pricing. In other words, to require NIH to do some an t that another provision was needed to achieve that end.

On 1

2/14/2016 5:17 PM, Rohrbaugh, Mark (NIH/OD) [E] wrote:

I was

just answering a question for a reporter and was reminded that t heregsrequireustoincludeinourexclusivelicensesthelice nsee’s requirement to “use its reasonable commercial efforts to bring the Licensed Products to Practical Application”.,wh ere "Practical Application" means to manufacture in the ca se of a composition or product, to practice in the case of a pr ocessor method, or to operate in the case of a machine or syst em; and in each case, under these conditions as to establish that the invention is being utilized and that its benefits aretotheextentpermittedbylaworGovernment regulatio ns available to the public on reasonable terms

If “reasona

ble terms” means reasonable price why did we need the reasonabl

e
p
r
i
c
i
n
g
c
l
a
u
s
e
a
n
d
w
h
y
w
a
s
t
h
e
p
o
i
n
t
n
e
v
e
r
r
a
i
s
e
d
i
n
t
h
e
1
9
9
0
s
d

iscussion that we already had that authority under the definit ion of Practical Application.

??

Not sure if I want to go publi

c with this?

What do you think?

From: Joe Allen [mailto:jal

len@allen.assoc.com] **Sent:** Wednesday, December 14, 2016 3:1

5PM **To:** Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV> **C**

c: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>**Su**

bject: Re: Comment replying to me

Just found that the even nu

mbered pages appear at the end of the document.

On 12/14/20

169:51 AM, Rohrbaugh, Mark (NIH/OD) [E] wrote:

Is this what y

ouarelookingfor:

"ProblemAreasAffectingUsefulnessofR

esults of Government-Sponsored Research in Medicinal Chemi stry"?

Sent from my iPhone

On Dec 14, 2016, at 9:04 AM, Joe Al

len <jallen@allen-assoc.com> wrote:

Were these drugs disc

overed with federal funds or just developed by the government after they were invented elsewhere?

Thanks

On 12/13/2016

10:34 AM, Rohrbaugh, Mark (NIH/OD) [E] wrote:

And there is the

poliovaccinewherethegovtbroughtitthroughclinicaltrial s, but these are rare examples and the regulatory requirements to bring drugs to market are far more extensive and costly then p re-KefauverHarrisAmendmentof1962requiringthatdrugsbesh own to be both safe and effective.

From: Joe Allen [mailto:j

allen@allen-assoc.com] **Sent:** Tuesday, December 13, 2016 10:

26AM **To:** Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>

; Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov> **Sub**

ject: Comment replying to me

Have to duck out but noticed that

someonerepliedtomycommentintheNYTimes.TheStanford-UC patent (Boyer-Cohen) was developed under the IPA program (ad ministrative Bayh-Dole) so I can rebut that one. Any thought s on his other observations? Thanks

Brisbane, Australia

11 hours ago" Before Bayh-Dole not a single new drug had been co

mmercialized from federally-funded research." Seriously

?This is a ridiculous statement. The first thing to note is tha tal most all drugs, even today, originate in publicly-funded laboratories. One only has to think of the most famous of the ma ll, penicillin which has probably had greater medical impact than any other. Its original discovery, by Fleming, then its l arge-scale purification and clinical testing (by Florey, Un iversity of Oxford) was entirely publicly funded before tran sferring to pharma companies for large-scale manufacture. D it to for the earlier sulfonamides, though first discovered b y Bayer its clinical application was in the Pasteur Institute thendefinitivelyatColumbiaUniversity(whoworkedwithph arma to obtain the chemicals). Or more recently, in the decade beforeBayh-Dole,thebiotechindustryhaditsgenesisatUCS

F-Stanford (and Harvard and a few other places). The UCSF rese archers created recombinant insulin and it became the founda tion of Genentech (along with Harvard's Biogen, the first bio tech companies). Ditto for Amgen's EPO, and dozens of others

- - JosephP.AllenPresidentAllenandAssociates60704Rt.26,Sou thBethesda,OH 43719(W)740-484-1814(c)

b6

www.allen-asso

c.com

- -

Joseph P. Allen President Allen and Associates 60704 Rt. 2

6, South Bethesda, OH 43719 (W) 740-484-1814 (c) b6 www.allen assoc.com

--

JosephP.AllenPresidentAllenandAssociates6070

4Rt.26,SouthBethesda,OH 43719(W)740-484-1814(c) b6 www.

allen-assoc.com

--

Joseph P. Allen
President
Allen and Associates

60704 Rt. 26, South Bethesda, OH 43719 (W) 740-484-1814 (c)

b6

www.allen-assoc.com

--

Joseph P. Allen
President
Allen and Associates
60704 Rt. 26, South
Bethesda, OH 43719
(W) 740-484-1814
(c) b6
www.allen-assoc.com

--

Joseph P. Allen
President
Allen and Associates
60704 Rt. 26, South
Bethesda, OH 43719
(W) 740-484-1814
(c) b6
www.allen-assoc.com

--

Joseph P. Allen
President
Allen and Associates

60704 Rt. 26, South
Bethesda, OH 43719
(W) 740-484-1814
(c) b6
www.allen-assoc.com

--

Joseph P. Allen
President
Allen and Associates
60704 Rt. 26, South
Bethesda, OH 43719
(W) 740-484-1814
(c) b6
www.allen-assoc.com

--

Joseph P. Allen
President
Allen and Associates
60704 Rt. 26, South
Bethesda, OH 43719
(W) 740-484-1814
(c) b6
www.allen-assoc.com